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CLINICAL DIFFERENTIATION IN THE SYNDROME CALLED ATYPICAL PNEUMONIA*

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IN recent years the introduction of the term "atypical pneumonia" to describe an allegedly new disease has resulted in much confusion in the differentiation of acute pulmonary inflammations. The nomenclature and classification of these diseases had always been complex and illogical; now they have become chaotic. Their contemplation makes one think regretfully of the simple pre-Morgagni era when all typical pneumonias were called "peripneumony"; those cases that departed from the prescribed pattern were deprecated and classed together as "bastard peripneumony". Similarly, pleurisy that did not conform was called "spurious". These vigorous terms reflect the exasperation that all clinicians feel when cases are unconventional in their behaviour. Even the pre-Roentgen days were happier than ours; acute inflammations were then classified as pneumonia or acute bronchitis, depending on the presence or absence of simple physical signs of consolidation.

The relative complacency of the last century has been destroyed by new knowledge in bacteriology and radiology. New facts in bacteriology and radiology have made the old clinical nomenclature obsolete. Bacteriology may ultimately provide the main background against which a logical classification of pulmonary infections will be made, but for various reasons, a purely bacteriological classification will never be completely adequate. There are still a large number of unknown viruses; even in the case of those that are known, identification is so slow and laborious as to be of no immediate clinical value. Even if we could identify the causative or predominating organism in every acute pulmonary inflammation, it would still be necessary to classify and describe individual cases on a clinical basis. This arises from the fact that each organism may produce a wide variety of local and constitutional effects. For example, "streptococcal pneumonia" may mean anything from an acute fulminating and rapidly fatal œdema to a mild localized infiltration. Furthermore, many pulmonary infections are not bacteriologically simple. Often more than one organism is involved and sometimes they predominate in turn. Even the course of a disease as specific as tuberculosis is much influenced by secondary invaders. Moreover the infective element alone rarely accounts for the complete picture; the predominating factor in many cases is not the infection, but emphysema, obstruction, allergy or vascular disease. For these reasons, clinicians will look to the bacteriologists in vain for a satisfactory classification. Certainly, it is of the greatest value to know what organism predominates but this information is subsidiary to the main diagnosis and should be recorded as such.

The principal addition to the knowledge of of acute pulmonary inflammation has been supplied by radiography. It has disclosed a large number of pulmonary infiltrations, the existence of which was unsuspected by older methods. Thousands of cases which were previously called "bronchitis" can now be shown to have areas of consolidation. It is in the differentiation and nomenclature of these that the chief difficulty has arisen. Radiographically they present a wide variety of shadows, most of which may simulate the appearance produced by well-known conditions, *e.g.*, lobar pneumonia, tuberculosis, abscess, neoplasm and bronchiectasis. The radiologists often refer to these shadows as "atypical pneumonia". Such a descriptive term is legitimate if the radiologist implies that he

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sees an infiltration which is not typical of pneumonia as he has known it. That is, he is saying what it is not, rather than what it is. Unfortunately, clinicians have frequently taken these radiological pronouncements literally and less critically than any candid radiologist would wish them to be taken. As a result a heterogeneous group of diseases has been treated as a single disease. In addition there is a tendency to group with them individual cases of well known diseases in which the opacities depart from the usual pattern. One frequently sees in consequence cases of tuberculosis, neoplasm, atelectasis, etc., treated for weeks as the benign though protean "atypical pneumonia".

Widespread and uncritical use of the term "primary atypical pneumonia of unknown etiology" has had a like effect. Careful clinical study of alleged examples of this disease will frequently show: (1) In the majority of cases they are not really "primary". (2) They are not atypical but may be subdivided into groups of cases which are typical for that group. (3) Clinically, they are quite dissimilar to any recognized pneumonia and have no more relation to the pneumococcus than to any other organism or virus. (4) Their etiology is no more unknown than that of many other medical conditions and their pathogenesis is often quite obvious.

What, then, are these lesions? There seems no doubt that they represent a heterogeneous group containing widely divergent types of cases. It is suggested that this large group can be easily subdivided by simple clinical study.

For many years, clinicians have given lip service to the proposition that inflammation in any part of the respiratory tract may lead to contamination and inflammation in any other part. Now that radiography has proved this to be a fact, not a theory, we are taken by surprise. We are but slowly coming to appreciate that the lung is indeed frequently involved in inflammatory processes which cast a shadow similar to what we had learned to consider as due to clinical pneumonia. Also it is evident that these infiltrations are associated with a wide variety of constitutional effects, physical signs and respiratory symptoms, the degree of which bears no regular relationship to the appearance of the radiological shadow.

CLASSIFICATION

There are at least nine separable groups of this so-called atypical pneumonia. This grouping cannot be done by bacteriological or radiological investigations but only by clinical study. The instrument of greatest diagnostic value here is a chronological account covering the antecedent period and the detailed history of onset. The classification that is offered is based on the belief that so-called atypical pneumonias are frequently secondary to some pre-existing condition which may be discovered by a careful history.

It is suggested that these infiltrations be called "pneumonitis" and not pneumonia. In a completely logical nomenclature, the word pneumonia would be limited to pulmonary inflammation produced by pneumococci, just as tuberculosis is inflammation due to tubercle bacilli. The word pneumonia has for centuries carried a specific clinical implication; it is an acute pulmonary inflammation with fairly constant signs and symptoms and a typical course. The group of conditions under consideration here is quite distinct from this. Moreover, by using pneumonitis as a generic term, there would be conformity with the plan of classification used for inflammation in other organs; it would be analogous to carditis, arthritis, hepatitis, etc. None of these are considered to be complete diagnoses but must be qualified; *e.g.*, "carditis, rheumatic, with mitral stenosis and congestive failure". So pneumonitis would simply imply inflammation in the parenchyma and the necessary qualifying terms must be added.

Following this plan the cases now commonly called "primary atypical pneumonia" can be divided into the following sub-classifications in accordance with their causes: (1) common cold pneumonitis; (2) influenzal pneumonitis; (3) contamination pneumonitis; (4) exacerbation pneumonitis; (5) atelectatic pneumonitis; (6) allergic pneumonitis; (7) pneumonitis due to known viruses and rickettsias; (8) pneumonitis due to unknown viruses; (9) miscellaneous.

1. *Common cold pneumonitis.*—Early in the war, recruiting boards encountered surprisingly gross pulmonary opacities in apparently healthy recruits. Investigation showed that most of these were associated with a common cold. There were no discoverable physical signs and very mild symptoms attributable to the pulmonary inflammation. Complete resolu-

tion occurred in the course of a few weeks. Major F. G. Stuart[1] has reviewed the chest films of 19,050 recruits taken in 1943. In 42 men (0.2%), evidence of "primary atypical pneumonia" was found. He states: "All recruits were ambulant, and at the worst, thought that they were suffering from 'bad colds' only. This suggests that at least 1 in 500 of the ambulant population is going about with an undiagnosed acute parenchymal inflammation of the lungs."

This came as a surprise to many of us but in an excellent paper in 1939 Ramsay and Scadding[2] cited many reports, going back to 1931, in which radiographic opacities of the lung associated with catarrhal infections, "grippe" and "influenza" are described. The authors did not, however, draw a distinction between influenza and the common cold.

It may be that this form of pneumonitis is due to the virus of common cold but evidence of this is still not conclusive and to label these cases "virus pneumonia" is premature. That they are not due to pyogenic organisms is suggested by the mild reaction, the absence of pus and blood in the sputum, and the normal leucocyte count. These lesions appear to be innocuous, but it is possible that they may contribute to the production of otherwise unexplained fibrosis.

2. *Influenzal pneumonitis.* — Epidemic or sporadic influenza may be followed by various types of pulmonary complications, as is attested by excellent clinical accounts going back for over a hundred years. Radiography has shown in the past few years that what the older writers called influenzal bronchitis frequently shows opacities. These lesions produce clinical manifestations which may vary from acute fulminating bronchopneumonia (as in the pandemic of 1918) to slight infiltration which is quite unsuspected until disclosed by x-ray. Post-influenzal pneumonitis can be differentiated from other forms only by discovering an antecedent history of influenza. There must be a sudden febrile onset with constitutional symptoms (headache, anorexia, weakness, general pains and mild chilliness) which persist for a few days; there are no localizing signs such as coryza, sore throat, dyspnœa or chest pain at the onset, but after some hours there may be subjective evidence of tracheitis. This type of onset contrasts with the local (nasal and pharyngeal) symptoms observed in the common cold.[3]

Serological tests may in some epidemics identify the influenza virus A or B;[4, 5, 6] but in many cases which must be regarded as clinical influenza, these tests are negative and other viruses appear to be responsible. The leucocyte count is normal, rusty sputum is absent, evidence of pleurisy is rare, physical signs are scant, there is no response to the sulfa drugs or penicillin, and the prognosis is uniformly good. That this type is not "primary" becomes quite evident during epidemics; then, in an influenza ward, one sees cases that are identical in all respects (history, symptoms, signs and course), except that some show radiological opacities. These latter are often called "primary atypical pneumonia of unknown etiology" in spite of the fact that they are obviously secondary to influenza, quite typical of influenza, and no more unknown in etiology than is influenza itself.

3. *Contamination pneumonitis.* — Every patient who has upper respiratory infection continually contaminates the whole of his respiratory tract, as is attested by the fact that lipiodol can be shown to be aspirated into the depths of the lung during sleep. The constant hazard of infection by aspiration is offset by the natural drainage forces of the lung; *i.e.,* respiratory "pumping", ciliary activity, the cough reflex, and also by phagocytosis and immunological activity of body fluids. When these mechanisms are intact much contamination may be countered; but if for any reason they are deficient infected material is trapped and may initiate pneumonitis. The clinical result varies widely with the organism involved, the extent of the inflammation and previous condition of the lung. Such an episode may occur once in the course of an acute upper respiratory infection and never recur; but it is probable that one such incident predisposes to others by causing permanent injury to drainage facilities. In chronic sinusitis such exacerbations may be frequent and account for many cases of so-called "recurring bronchitis". These acute episodes are commonly diagnosed as pneumonia, acute bronchitis, or pleurisy. They may be identified by the antecedent history of acute or chronic upper respiratory infection and by the fact that they do not conform in general clinical characteristics to acute lobar pneumonia or to idiopathic pleurisy. It has been noted[7] that the radio-

logical shadow associated with sinusitis is of a more extensive bronchopneumonic type as contrasted with the lesser ground-glass type of lesion seen with simple coryza. The striking unanimity of observers[7 to 10] in describing the predominance of shadows in the lower lobes in "atypical pneumonia" suggests that some of these lesions are the result of aspiration.

4. *Exacerbation pneumonitis.*—Any pulmonary inflammation may result in residual fibrosis whereby an area of the lung is left with impaired drainage and blood supply and is therefore more susceptible to recurrence of inflammation. Such vulnerable spots may blaze into varying degrees of activity whenever they become contaminated by a new infection. These acute episodes punctuate the history of almost every bronchiectatic. They are indeed the chief factor in the pathogenesis of full blown acquired bronchiectasis. The history is usually one of repeated "pneumonia", "pleurisy", or "bronchitis"—always in the same base. These attacks are bizarre in their clinical manifestations, varying from what may be called "a cold in the chest" to something that may resemble acute pneumococcal pneumonia. These are the cases commonly diagnosed "unresolved pneumonia", because physical and radiologic signs persist after the acute attack has subsided. They are areas of subacute or chronic inflammation which from time to time become obvious because of a temporary "flare-up". The site of the lesion may often be found between acute attacks by evidence of fibrosis. Persistent localized post-tussic crepitation is the most constant sign and may be present in the absence of diagnostic radiologic evidence. During acute attacks these cases are usually called "atypical pneumonia". In one account[10] of 500 cases of primary atypical pneumonia bronchiectasis was found to be present in almost 2%. Those not arising from the pneumonic process itself may be separated as a group by the recurring history and persistence of physical and radiographical signs of a region of fibrosis. Evidence of definite bronchiectasis may or may not be found by bronchography.

5. *Atelectatic pneumonitis.*—The extent to which actual bronchial obstruction contributes to the production of various acute pulmonary inflammations has been the subject of much discussion in recent years. Some believe that it is a main feature in the pathogenesis even in lobar pneumonia. This is usually regarded as an extreme attitude and most observers do not presume obstruction except when history, physical signs, and x-ray findings are characteristic.

The most common example of obstructive pneumonitis is so-called "post-operative pneumonia" which is now universally considered to be due to mucous plugs and spasm with consequent atelectasis. Other common causes of obstructive pneumonitis are hæmoptysis, neoplasms, foreign bodies, and aneurysms. But there are cases that arise acutely and are quite unrelated to these conditions, due to aspiration of muco-purulent plugs in relatively healthy people. It is worth while recognizing such cases because the general principles underlying treatment are totally different from those applied to purely inflammatory lesions. The proof of such cases is by x-ray; it will show evidence of atelectasis; *i.e.*, elevation of the diaphragm, shifting of the mediastinum and, in severe cases, depression of the ribs on the side of the lesion. The lesion itself is usually homogeneous, though it may be mottled or stringy. The collapse is almost always limited to the lower lobes or the right middle lobe. When a lower lobe folds, it produces a triangular shadow posterior to the heart shadow or in a corresponding position on the right side. If the middle lobe is affected, it produces a triangular shadow based on the hilum. Collapse of part of a lobe may produce less characteristic shadows; often they are lenticular and horizontally placed.

Such obstructive lesions may be suspected on the history and physical examination. It is common to find one or more of the following: (*a*) a history of chronic or sub-acute upper respiratory infection going back for some weeks or months. This is the source of the plug. (*b*) The onset is usually sudden and dominated by pain, dyspnœa and cough rather than by fever and constitutional symptoms; there may be purulent expectoration and some blood. (*c*) Constitutional symptoms are mild and the temperature is not high at first, but may develop if the obstructed area is large and heavily infected. (*d*) Physical signs are usually confined to the medial third of one base behind or to the surface of the middle lobe in front. (*e*) Besides the x-ray findings characteristic of atelectasis, there is frequently some evidence in the film that embarrassment to pulmonary drainage may have existed before the acute episode. This may be suggested by gross calcification in

the hilum or lung, old adhesion of the diaphragm or some fibrosis.

In some cases the obstructive origin of the lesion may be quite obvious, in others it can only be suspected. It is important to recognize its possibility so that steps to dislodge the plug may be taken.

It is obvious that the three last groups, *i.e.*, contamination, exacerbation, and obstructive pneumonitis, are not mutually exclusive. Each, of course, depends primarily on contamination and the amount contributed in a given case by previous lung damage or by obstruction is often not easy to judge. In spite of this, the terms have been found useful in creating a logical point of view and to direct interest in treatment and prognosis along rational lines. A large proportion of cases fall quite readily into one or other of the groups. For example, pulmonary infiltration following an acute or chronic upper respiratory infection in a patient who has no history or signs of previous inflammation must be regarded as simple contamination and fortuitous trapping. If there have been several attacks at the same site and there is evidence of local fibrosis, the term "exacerbation" emphasizes the main feature in the pathogenesis. If the evidence suggests that obstruction is playing a major part, it is highly important that this should be recognized in the diagnosis. Certainly, the practice of including them all under one diagnostic term—atypical pneumonia—contributes to vague thinking, superficial investigation, inadequate treatment and faulty disposal.

6. *Allergic pneumonitis.*—In every pulmonary infection an effort should be made to estimate what contribution allergy is making. Allergic pneumonitis is occasionally seen in the pure form and is commonly called "Loeffler's syndrome". In this, a circumscribed "ground-glass" x-ray shadow appears and disappears suddenly and is associated with eosinophilia and relatively mild general and local effects. Other less definite allergic lesions are common. In patients who are subject to asthma, various sorts of pulmonary opacities occur from time to time. In these it is usually difficult to determine how much is due to obstruction from spasm and abnormal secretion, how much to inflammation, and how much to allergy. Very widespread "bronchopneumonic" infiltration may often be found in asthmatics with surprisingly mild symptoms and may therefore be assumed to be mainly allergic.

7. *Pneumonitis due to known viruses and rickettsias.*—A diagnosis in this group can but rarely be made in this country. The infiltration that may complicate the common cold, influenza, and Stevens-Johnson syndrome may be presumed to be due to the viruses of those diseases, but this is still unproved in human cases. Psittacosis, ornithosis and the rickettsias may produce a syndrome clinically indistiguishable from primary atypical pneumonia but these agents are almost unknown in Canada. The pulmonary complications of measles, variola, varicella, vaccinia, lymphocytic choriomeningitis and lymphogranuloma venereum may be due to their specific viruses, but in any case, other manifestations of the diseases serve to identify them.

8. *Pneumonitis due to unknown viruses.*—It was the recognition of the syndrome caused by this group which stimulated the great interest in "primary atypical pneumonia" which has been in evidence for the past decade. As with any new diagnosis there has been a tendency to overuse it; the time has now come to restrict its application to a well delineated entity. This may be done by eliminating the causes of pulmonary infiltrations already considered and also by ensuring that this diagnosis is made only when the clinical picture meets the requirements to be described.

Though it appears likely that this disease has been prevalent for many years[2, 8, 9] it was not until the papers of Gallagher,[11] Bowen[12] and Allen[13] that this illness began to be properly differentiated. Since that time many papers have appeared describing the syndrome under a wide variety of names, but nonetheless agreeing on its essential features. The clinical picture so far has been restricted to cases with evidence of pulmonary involvement although it seems likely that these represent a minority of the patients infected by these agents. The usual syndrome consists of the insidious onset of constitutional symptoms (fever, headache, malaise), followed by cough, retrosternal soreness and mucopurulent sputum which may be blood streaked. Physical examination reveals little except fever, relatively slow pulse, pharyngeal injection and possible râles over the affected area. The leucocyte count is normal. The x-ray shows an infiltration which is variable in size, location and character, but usually out of proportion to the clinical picture. The

rise in cold agglutinins which has been noted in many cases is of diagnostic assistance when present. The conditions most apt to be confused with it are influenzal pneumonitis and common cold pneumonitis.

The virus etiology of the disease is now fairly well established. A number of investigators[14 to 16] have succeeded in obtaining various viruses from cases, and the disease has been induced in human volunteers by means of bacteria-free filtrates of sputa and throat washings.[17]

9. *Miscellaneous causes of pulmonary infiltrations.*—There are a number of other circumstances which produce pulmonary infiltrations which may resemble those of pneumonitis. Among these are infarcts, thromboses, neoplasms, mycoses, leukæmias, Hodgkin's disease, malaria, rheumatic fever, Boeck's sarcoid and inhalation of irritants. It has been assumed throughout that acute lobar (pneumococcal) pneumonia and the bacterial bronchopenumonias have been eliminated. When these latter have been modified by early chemotherapy their precise identification may be difficult.

COMMENT

The foregoing classification is applicable only to cases in which parenchymal involvement is present. The criterion of this in practice is a radiographic shadow. It is quite probable that mild degrees of parenchymal infiltration may exist without producing a definite shadow. It is also likely that any of the primary conditions referred to, *e.g.*, common cold, influenza, etc., may produce lesions in the lung that do not progress to actual consolidation. Indeed, in practice, one frequently sees cases arising under circumstances that could produce pneumonitis with signs and symptoms that suggest its presence, but in which the radiogram is negative. Such cases can only be called acute bronchitis or tracheitis as the signs and symptoms suggest. It is evident that the two groups (pneumonitis and acute bronchitis) merge imperceptibly when judged clinically; it seems likely that this is also true of their actual pathology.

SUMMARY

1. The confusion in nomenclature and classification of acute pulmonary inflammations since the advent of the term "primary atypical pneumonia" is deplored.

2. It is suggested that the generic term "pneumonitis" be adopted to describe these infiltrations. Nine groups or subclassifications are recommended and the diagnostic criteria of each are indicated.

3. In particular, the diagnosis of so-called "primary atypical pneumonia" should be made only after a careful differentiation from other easily recognizable entities has been made. This should make for clearer concepts, more accurate diagnosis and better treatment.

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THE USE AND LIMITATIONS OF HEARING AIDS*

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THE observations made in this paper are based on the examination of 750 hard-of-hearing individuals referred by the National Society of the Deaf and the Hard of Hearing during the past five years, for an opinion as to what help could be expected from an aid.

A routine otological report was used which included relevant history, ear, nose and throat examination, audiometric and standard speech tests, and, when indicated, investigation of patency of Eustachian tubes.

One of the available aids was then fitted, and the change in threshold noted on the audiometer, and also the amount of increased loudness above threshold that could be tolerated at each frequency. The speech tests were then repeated with the aid, and the degree of improvement noted. No attempt was made to advise any one make of instrument, but only

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to indicate whether the degree and type of loss of the individual would permit him to get sufficient help from any aid to justify purchase, and what type would be most satisfactory. If an aid were bought, they were asked to report later the degree of satisfaction obtained in everyday use.

In determining how much a hearing aid will help a deafened individual we have to consider three factors: (1) The characteristics of speech sounds. (2) The way in which these are altered by the aid. (3) The ability of the damaged auditory tract to tolerate and transmit enough of the altered speech to the cortex to give understanding either alone or in conjunction with lip reading.

CHARACTERISTICS OF SPEECH SOUNDS

Speech is roughly made up of sound waves, the frequencies of which range between 300 to 3,000 vibrations per second. The loudness of average speech ranges between 30 to 60 decibels. While speech patterns are very complex, they have certain broad characteristics, an understanding of which is useful in translating frequency loss into ability to follow speech. While it is not true that the vowel sounds all come in the lower part of the speech frequencies and the consonants in the higher, nevertheless, as shown by Fletcher, the vowels and consonants do to a large extent have their predominant characteristics in these respective regions and a man with a high tone loss will tend to miss more consonants and vice versa. In addition certain combinations of vowels and syllables fall into the higher range group, and others into a lower range group, and these factors are made use of in speech testing.

Consonants, on the whole, also are quieter and shorter than vowels and are therefore harder to hear even with a flat curve loss, and first to be missed in early deafness. On the other hand this is compensated for to some extent by the fact that they are usually the easiest sounds to lip read.

HOW SPEECH IS ALTERED BY A HEARING AID

Loudness may be increased by as much as 50 decibels. A certain degree of distortion may be present, the degree increasing according to the loudness of the input, and the degree of attenuation. Most good aids have but little distortion till the output approximates 120 decibels.

Certain variations in tone can be obtained by special filters and varying the receivers. Bone receivers accentuate lower tones which tend to mask the higher tones. This makes the voice sound louder and deeper, but at the expense of intelligibility because the more important consonants are missed.

Crystal ear receivers are more sensitive to slight variations, but may be affected by atmospheric conditions. Magnetic receivers are less sensitive but being less subject to change are more reliable.

All aids will cause feed back squeal at full volume, unless the ear piece fits tightly. For this reason it is important to have an individually moulded ear piece, particularly in those cases with severe losses.

EFFECT OF AUDITORY DAMAGE

The ability of the damaged auditory tract to utilize the sound delivered by the aid to the canal varies greatly, and while many factors are involved the chief ones are: the degree of loss in each of the speech frequencies, and the amount of nerve damage as indicated by drop in bone conduction and intensity tolerance. By measuring these and considering them in relation to other factors such as age, duration, lip reading ability, intelligence, occupation, etc., one can give fairly sound advice as to whether an aid can be worn with satisfaction and what type is most suitable.

(*a*) *Degree of loss.** — As mentioned previously, average speech at conversational distances varies in loudness between 30 to 60 decibels. Thus those with losses below 30 decibels will not have much trouble with ordinary day-to-day conversation, but may have some difficulty at lectures, church, theatres, etc., if too far back.

Those with losses between 30 to 40 decibels will miss the quieter speech sounds, chiefly the consonants and unstressed syllables. They complain that people are mumbling, and find lip reading very useful. They have definite trouble hearing beyond 10 feet and will find an aid useful for distance as in assemblies.

Those with losses between 40 to 50 decibels will tend to miss some of the vowel sounds also. They cannot follow conversational voice beyond 5 feet, and will usually have enough trouble at conversational distances to require

* In discussing decibel loss reference is made to the average loss in the speech frequencies.

an aid for every-day use though they will often refuse to admit it.

Those with losses greater than 50 decibels will definitely require an aid and usually accept the fact.

(*b*) *Frequency variation.*—As the consonants tend to lie largely in the upper portion of the speech range, it is apparent that those with maximum loss in the high tones, as is usually the case with nerve deafness, will tend to have greater difficulty with the consonants. The opposite is true where the loss is more in the lower tones. If the difference of the threshold between the low and high tones is very great, it is difficult to increase the loudness of the high tones sufficiently without making the lower tones too loud, and those with this type of loss usually have to rely on lip reading. The same difficulty arises where there is a marked irregularity of the curve in the speech range, but it is remarkable how individuals with this type of loss can learn by auricular training to interpret speech very accurately without an aid even when heard in this distorted manner.

(*c*) *Degree of nerve involvement.*—With nerve damage, recruitment comes into play so that the loudness at which a sound is heard increases in much greater proportion with increased intensity than is the case with a conductive loss, so that the range of loudness between where a sound is first heard and where it becomes uncomfortably loud may be quite narrow. It is this degree of tolerance that is the most vital factor in determining the amount of practical help that can be expected from an aid. Loudness of speech varies as much as 30 decibels even when spoken at a fixed distance, but, as it is necessary in every day life to be able to hear different voices at varying distances, a much wider range of loudness must be tolerated in order to get ideal hearing. It is apparent therefore that with an individual who has only a tolerance of 15 decibels so large a proportion of speech will be either too quiet to be heard or too loud to be tolerated that he will get no practical help.

It is this type of patient who can be influenced by a dealer, who may test them in a quiet room at a fixed distance and using a monotone, into purchasing an aid that he will find of little practical value in day-by-day life situations. When the tolerance is around 30 decibels, it is found that, other factors being equal, the patient can get limited help in quiet surroundings but he will have to adjust his volume control frequently according to the distance and loudness of the speaker's voice.

When the tolerance is 60 decibels or more it is usually found that an aid can be used with satisfaction in all ordinary environments.

In the cases studied it was found that, while each had to be considered as an individual problem because of the many variables, they could be divided into broad groups.

1. Patients with little or no nerve involvement and fairly flat audiogram. These are characterized by good bone conduction and wide dynamic range. This is the ideal group for an aid. They will get good intelligibility with any aid with very little difference between one aid and another provided the power is suited to their degree of loss. They can get satisfactory results in most ordinary environments. Their limitation is that of mon-aural hearing with inability to discern the direction of the sound source or to identify the voices when several are talking at once.

They should be encouraged to wear an aid as early as possible because there is reason to believe that the nerve degeneration that occurs later in some of these cases may be an atrophy of disuse due to lack of stimulation of the end organ, and if so this can be avoided by using amplification to keep the cochlea functioning. It will also help to avoid speech changes. Fit poor ear if patient has usable hearing in better ear and intelligibility and tolerance satisfactory. Fit good ear if the loss is 60 decibels or more, or if tolerance is not adequate in poor ear.

If bone conduction is indicated fit the ear with best bone conduction regardless. They will usually get better intelligibility with an air receiver but a bone receiver is indicated where there is: (*a*) Chronic purulent otitis media in ear to be fitted. (*b*) Severe chronic eczematous otitis externa in ear to be fitted. (*c*) Those cases of otosclerosis where there is considerable stapes fixation and little nerve involvement. These cases will show better intelligibility to speech tests with bone receiver. (*d*) Better intensity tolerance by bone conduction.

2. Patients predominantly of a nerve type with poor dynamic range. In this group their hearing increases greatly with loudness and there is a sharp demarcation between when

they hear and when they do not. If their degree of loss is only moderate, *i.e.*, less than 40 decibels, they hear all the louder sounds of speech very well, (chiefly vowels) but miss the quieter sounds completely (consonants). They learn in time to translate speech amazingly well from just hearing the louder sounds, and usually consciously or unconsciously learn to fill in the gaps with lip reading. There were a very large number of this type in our series as compared with work done at the Rehabilitation Centre of the Deaf and Hard of Hearing at Deshon General Hospital, U.S. This is probably due to the fact that in the army all cases are seen, and they are in the younger age group before much nerve deterioration has set in.

On the other hand patients applying to the National Society are chiefly the problem cases: those who have tried aids without satisfaction and therefore largely those with a fair amount of nerve involvement including many with presbycusis. It was found that members of this group have great difficulty in wearing an aid, and the amount of help that can be obtained is proportional to the degree of tolerance at the speech frequencies. This can be measured with the aid and often varies in the different frequencies, the tolerance usually being less in the tones with the lowest threshold.

This poor tolerance raises two important questions. (1) Will wearing an aid that must necessarily exceed the loudness limit of comfort if it is to get intelligible speech to the cortex further increase the nerve damage? (2) Can the tolerance be increased by gradually increased power?

From the experience gained the answer to both of these questions is "yes". Patients have been observed over long periods who had progressed slowly to the point where they had started to wear an aid and then showed a definite increased drop. To offset this, it was found that while their ability to hear without the aid was often decreased, their ability to tolerate the aid improved within certain limits.

In view of these findings it would appear wise in cases with moderate loss, perceptive in type, as indicated by a poor intensity tolerance, to withhold an aid until they are no longer able to carry on satisfactorily without it, and then to wear an aid with minimum power that will enable them to carry on in conjunction with lip reading, and that will accentuate tones with best tolerance. Sacrifice intelligibility for wearability, gradually increasing power as tolerance is increased. These are the ones that require considerable encouragement and follow-up to see that they persist until their tolerance increases and their intelligibility improves by auricular training to the point where an aid becomes an asset rather than a nuisance.

The help obtained will always be limited in these cases, but limited help is better than no help at all, and it has been surprising to see how patients with extreme losses (95 to 100 decibels) and practically no intelligibility with an aid alone increased their understanding to a marked degree when using an aid in conjunction with lip reading as compared to lip reading alone.

3. Children deaf since infancy. These cases, whether their deafness is congenital or acquired, present a more complex problem. None of them when an aid is first put on, whether it be done at 5 years of age or 20, will get much apparent intelligibility. This is, of course, due to lack of speech understanding. Never having heard speech sounds as we hear them, they are just as unintelligible as Greek is to us. If these children as soon as they are old enough to cooperate are tested with an aid on, by pure tones, it can be determined whether: (*a*) the threshold of the speech frequencies is raised enough to let all or part of speech sounds through; (*b*) whether there is enough tolerance above threshold to permit them to wear an aid in ordinary surroundings. If so, the child should, when exposed to this attenuated speech for definite periods for a length of time, learn to understand as well as a person with a similar loss occurring after such was acquired.

Further it is of vital importance that these children be exposed to speech in the earlier years when speech learning is most active, 3 to 6, as the longer it is left the more difficult it is to learn, and the less chance they have of keeping up with their own age group educationally. Those who have not enough residual hearing to benefit in this way will have to carry on with lip reading or other methods until a portable machine is available for transmitting speech sounds into a readable visual speech code such as the one that the Bell Telephone Company are now experimenting with on a large scale.

PRESBYCUSIS

These individuals having heard well until their latter years are unable to make the adjustments that come about with a gradual loss over many years. They have not learned to lip read, and are past the age when they can readily do so. Their deafness is of a nerve type with poor tolerance so that they could expect only limited help in quiet surroundings. In addition they are past the age when their hearing apparatus can adjust itself to the repeated attacks to their discomfort threshold as a younger individual is able to do to some extent, and the aid is apt to be more of a nuisance than a help. Consequently only those cases who show good intelligibility and fair tolerance from the start should be advised to wear an aid. The rest are better off with the cupped hand, trumpet or speaking tube, depending on their degree of loss.

TINNITUS

Occasional patients were seen who though having good intelligibility and a deafness that was predominantly conductive, as indicated by good bone conduction and wide dynamic range, found that wearing an aid tended to increase their tinnitus to a degree that made the aid intolerable. This was found to be less troublesome in some of these when a bone receiver was used, even though the intelligibility was slightly diminished.

A persistent tinnitus also has a tendency to increase the handicap by its masking effect. It is helpful to measure the pitch of the tinnitus with the audiometer as a low pitched tinnitus will mask speech more than one of high pitch, and is harder to become adjusted to.

PSYCHOLOGICAL ADJUSTMENTS

This was found to be one of the greatest difficulties and particularly in the younger patients with moderate losses. The reasons for this are: (*a*) the deafened individual wants to hide his loss, as it is apt to be regarded by others as stupidity because of misunderstanding and inability to follow instructions, and as a nuisance because of the necessity of repeating and shouting. (*b*) He appears perfectly normal so far as the general public is concerned until he labels himself as deaf by wearing an aid. It is only when the embarrassment of the loss becomes great enough to outweigh the embarrassment of having it apparent for all to see that an aid will be accepted, and thus many refuse to wear one till long after it is needed. This may seem stupid to a normal-hearing individual, but it is a very real thing and cannot be easily brushed aside.

It is sometimes helpful to make them aware of just how much they are not hearing. Most of them, because of wishful thinking and because what they do not hear they are not aware of missing, convince themselves that their hearing is much better than it is though the true loss is only too apparent to their family and friends. It can be explained that an aid makes them much less conspicuous than being shouted at and making embarrassing mistakes. Often they can be persuaded by pointing out that it is selfish not to wear one because of the annoyance and embarrassment to their family and friends who have to keep repeating and shouting.

In the case of women, many of them will accept a bone receiver because they can more readily hide it with their hair, and when dealing with a sensitive individual I think it is wise to advise this, provided they can get reasonably good results, rather than bullying them into wearing an air receiver, which though it may be a little more efficient will be harder on their morale. However, if the difference in performance of the two receivers is very definite, the more efficient receiver should be chosen regardless.

With reference to school children, it should be noted that less psychological trauma will exist if they are in a class with other hard-of-hearing children with their own aids, or a group aid, than is the case if there is only one with an aid in a normal class. However, the necessity for an adequate education is paramount and each case must be handled according to the means available.

CONCLUSIONS

The limitations of a hearing aid are largely those imposed by the type of loss rather than by the acoustic imperfections of the aid. It is dependent largely on the degree of nerve involvement and the linear distortion of the loss. Between the pure conductive type with level curve who get immediate appreciable help with any good aid and the extreme nerve deafness type that get no practical help, there is a large borderline group of mixed deafness with a greater or lesser degree of nerve involvement

and linear distortion. It is the responsibility of the otologist to see that all of this group who have a suitable degree and type of loss to get practical help from an aid without increasing their loss, are urged to purchase one and persist with it until adequately adjusted to its use.

It is also his responsibility to see that those whose ear disease is such that they cannot adequately utilize attenuated speech are discouraged from spending time and money hopefully trying and buying every new model that comes on the market. The number of these borderline cases that are able to benefit can be increased if the following points are observed: an aid chosen with an eye to tolerance rather than intelligibility; if adequate use is made of lip reading to fill in the missing consonants; if auricular training is given to compensate for linear distortion; and use and power of the aid gradually increased to improve tolerance. This requires an accurate measure of the degree and type of loss, the choice of an aid with suitable power and frequency response, with competent servicing and follow-up, and encouragement to see that they persist to the point where their aid becomes psychologically and acoustically acceptable, and socially and economically beneficial.

CHRONIC EMPYEMA

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CHRONIC empyema has never been a popular subject for discussion at a general surgical meeting, and now it might even seem quite unnecessary since post-pneumonic empyema, the group with which we are most concerned, has been so successfully prevented by the present day treatment of pneumonia. In fact, post-pneumonic empyema has become so rare that it is safe to say that the majority of surgeons have not treated a single case during the past year. On the other hand thoracic surgeons are agreed that it is again time to discuss this subject; because, if there has not already been a relative increase of chronic cases, at least there has been a dangerous delay in instituting surgical drainage.

Two obvious reasons account for this increased proportion of delayed cases. (1) The few remaining empyemas have followed pneumonia so mild or so atypical or have occurred in patients living in such remote districts that the pneumonia was untreated; hence the empyema was not recognized until late. (2) Due to the success in the treatment of the primary lesion with penicillin it has been assumed that the complication could be cured with equal success. And this opinion has been reinforced by the report of many successes; but these have been largely in the earliest effusions before thick pus has given evidence of the formation of an actual empyema or walled-off abscess cavity containing fibrin and surrounded by a capsule.

The treatment of empyema always involves two factors; namely, the bacteriological agent and the physical or mechanical factor. Sterilization of the cavity is important but this alone neither avoids the danger of later chronic empyema nor assures the full restoration of function. The pus must be evacuated and the pleural cavity closed.

In 1896 Stephen Paget[1] published a textbook on Surgery of the Chest and now, fifty years later, the following statement from it is of some interest:

> "It is sometimes said that surgeons fifty years hence will think as little of our results as we think of the methods of fifty years ago. So far as regards the surgery of the chest, this is utterly untrue. Fifty years ago, it had risen only above the horizon, it is now nearly at its zenith."

However the quotation from this volume which I wish to use particularly is as follows:

> "It is impossible to understand how the Hippocratic treatment of empyema became so hopelessly lost; if it is true that Galen invented the aspirating syringe this was probably the beginning of the evil."

Some of you will remember that at the 1941 meeting of the Thoracic Surgery Association in Toronto it was considered necessary to sound the same sort of warning about the treatment of empyema with the sulfonamide group of chemicals; and now apparently there has been adequate experience with penicillin to realize that even this most effective therapeutic agent has proved inadequate on account of the peculiar physiology of the pleural cavity. As early as October, 1944, our president, Dr. Ray F. Farquharson,[2] in his address on penicillin before this College stated that "Surgical drainage was undertaken when the infecting organism persisted after the fourth injection of penicillin or when the pus was loculated, or too thick to be withdrawn through a needle."

A superficial survey has convinced me that the medical services under our Governmental

Departments have recently been adequately instructed in even wider application of the surgical treatment of empyema. Blades[3] representing the same opinion in the United States reports that surgical drainage became necessary in 20 out of 24 penicillin treated cases. He stressed the fact that surgical drainage carries less hazard than conservative treatment, if the latter requires upwards of a dozen aspirations and injections, even if prolonged non-operative treatment did produce a cure. In fact, such opinions are so well crystallized that discussion can only re-state and emphasize them.

CAUSE OF CHRONICITY

In reviewing the causes of chronicity in empyema it would seem to be missing the point to simply repeat the usual list—foreign bodies, lost tubes, osteomyelitis, bronchial fistulæ and intrapulmonary fibrosis due to bronchiectasis, stenosis, lung abscess or tuberculosis. In the majority of patients the major factor is simply improper treatment of the early stage, or more explicitly, (1) delayed drainage; (2) inadequate drainage; and (3) uncontrolled cessation of drainage.

The etiological factors usually mentioned are in most cases the result of improper drainage or at most only secondary additions to the major problem produced by the fibrous wall of the abscess cavity, the thick scar on or in the pleura due to the delay in evacuating the abscess cavity.

Delayed drainage. — Under the heading of delayed drainage as an important cause of chronicity, it would seem wise to mention the necessary short period of delay before creating an open pneumothorax in streptococcus empyemas. This may be important in the near future, for epidemiologists have expressed their belief that a widespread influenzal epidemic is near at hand. For this group Evarts Graham[4] and his associates defined fundamental principles after the first World War, when they warned against too early open drainage before the mediastinum had become fixed by fibrosis and adhesions. This is most important in the streptococcus group because in these patients the toxicity is still great and the vital capacity still low on account of a concomitant pneumonia in contrast with the pneumococcus group in which the empyema usually occurs after the intrapulmonary lesion has subsided.

But even in streptococcus empyema the optimum time for open drainage is relatively early; and prior to this the empyema cavity should be kept as empty as possible by aspiration so that when the abscess cavity is formed, the surrounding sear and adhesions will not hold the lung firmly against the mediastinum, thus producing a total pyothorax. During this early period intrapleural penicillin should play a most important part, so long as this procedure is not carried beyond the time that thick pus has formed, even though the pus be sterile. Smears and cultures of the fluid must be taken before intrapleural injections, and if possible before even systemic penicillin. After penicillin has been used in any way, cultures are liable to be sterile and even direct smears doubtful, thus causing inevitable confusion with tuberculous empyema which, of course, should be treated entirely differently.

Inadequate drainage.—Under the heading of inadequate drainage we should begin by visualizing the empyema cavity as simply an abscess. When the empyema is opened the fibrous wall of the abscess contracts, and with the aid of the pressure within the lung due to coughing, etc., pulls the lung and diaphragm toward the opening in the chest wall. In our small series of chronic cases we have been impressed with the difficulties encountered by drainage from too low a level. When the diaphragm rises it tends to isolate the low opening in the costo-phrenic angle. This point has been mentioned, but unusually dependent drainage, we believe, has been overstressed. Again, the use of small tubes, not large enough to evacuate thick pus and fibrin, has caused intermittent rather than the essential continuous drainage.

By following these simple principles we have had little need of using complicated apparatus for increased negative pressure, for tidal irrigation, specially designed tubes or special irrigating solutions. Occasionally the precaution of a water seal may be used for a few days. But as pointed out by Evarts Graham[5] in the continuous argument between open and closed drainage, the simple dressing, soon wet with pus, acts as sufficient valve to give all of the advantages of complicated closed systems.

Uncontrolled cessation of drainage. — The third, and in our experience, the most important cause of chronicity in the past has been the uncontrolled cessation of drainage. Without the experience of the last fifteen years I would not

believe possible the conditions that we have encountered; drains not larger than 20 French catheters; drains removed in two or three weeks without control by either x-ray or irrigation; and one case treated by an intercostal incision without the insertion of any tube.

TREATMENT OF CHRONIC EMPYEMA

At present a survey of the history of the treatment of chronic empyema would seem to be the tracing of a fifty year cycle. Everyone is familiar in name at least with the Estlander and Schede types of operation and the Fowler and Delorme decortication of the pleura. The former operations, by removing the ribs and thickened parietal pleura, attempted to collapse the softened wall down to the non-expanding lung. Decortication attempted to allow re-expansion of the collapsed lung by removal of the visceral pleura. Nearly fifty years ago these operations fell into disrepute on account of their high mortality rate. Consequently the conservative reaction back to simple drainage took place. About twenty-five years ago Hedbloom[6] reported a series of 300 cases of chronic empyema treated by drainage alone, but by wide open drainage replacing the inadequate treatment which had caused the chronicity. He reported 74% of cures by this simple therapy. Four years ago a similar series was reported from the Mayo Clinic[7] with similar results. Over 70% were cured by drainage alone or drainage combined with a minor plastic procedure.

The majority of thoracic surgeons have adopted a middle course. The first operation which consists only of correcting or re-establishing drainage by tube, by pack, or both, through a large opening, should be followed if necessary after three or four months by a plastic procedure much less extensive than the original Schede thoracoplasty. If, after three or four months, re-expansion has ceased, the residual empyema cavity, now usually quite small, can be completely unroofed. The removal of four or five inches from four to five ribs usually will be sufficient to accomplish this; and sometimes considerably less will be required. Enough rib and pleura should be removed to saucerize the cavity. In a few cases the space may be filled with skin and muscle flaps but as a rule the cavity will be small enough to leave open to granulate. In difficult areas, as under the scapula or in the paravertebral gutter, pedicle muscle packs may be necessary.

During the past three years under the leadership of the American Army chest surgery units[8, 9] in the Mediterranean, a most significant change has taken place in the treatment of empyema. Working at first with sterile clotted hæmothoraces and later with infected hæmothoraces they demonstrated at least three most important facts.

(1) The outer layers of the clotted hæmothorax or empyema cavity form a fibroblastic deposit on the pleura. That is, the so-called thickened pleura is at first only a fibrinous or fibrous layer on the pleura rather than a thickening of the pleura itself. Although this fibrinous deposit shows definite fibroblastic and angioblastic activity as early as two weeks, yet it does not have an organic fusion with the pleura until from eight to ten weeks. (2) Prior to the introduction of penicillin it was shown in sterile hæmothorax cases that this fibroblastic membrane could be "peeled" off the visceral pleura, resulting in immediate and complete re-expansion of the lung. (3) In March, 1944, under the protection of penicillin the same surgeons began to apply this principle to post-traumatic empyema with equally good results, if done in the period between two and ten weeks after the injury. And this was accomplished with a very low mortality rate. More recently the same treatment has been used for post-pneumonic empyema.[10]

Thus after fifty years the Fowler-Delorme decortication has been revived as a result of war-time studies of hæmothoraces and as the result of the introduction of penicillin.

Although sufficient time has not elapsed to estimate the value of this work as applied to post-pneumonic empyema in civilian practice, yet it might seem hard to understand why it should not be applied at least during this transition period between the acute and chronic stages, between about four and ten weeks. Some will undoubtedly feel that even these time limits can be extended; but, before adopting too wide an application of these principles, the following two facts stressed by the original workers should be remembered.

1. Post-traumatic empyema, because it is the result of infection of a hæmatoma, may have a thicker fibroblastic membrane than does a post-pneumonic empyema. This probably explains the greater difficulties in obtaining complete re-expansion of the lung in post-traumatic empyema as compared with post-pneumonic. For this

reason in post-pneumonic cases relatively early decortication may not be quite so necessary.

2. The original workers considered that early decortication played its greatest part in the treatment of total collapse or apical collapse. Patients with partial empyema, if limited toward the base, do sufficiently well after simple drainage during this transition period between the acute and chronic stages.

SUMMARY

1. The fundamental principles of the treatment of acute empyema have been reviewed as they influence the causes of chronicity.

2. A brief review of the treatment of chronic empyema has been outlined.

3. Three important changes in the empyema problem due to the introduction of penicillin have been mentioned. (*a*) Acute post-pneumonic empyema has become a rare condition in civilian practice. (*b*) There is still danger of undue delay in instituting adequate surgical drainage. (*c*) Thorough decortication is now possible with a low mortality rate, at least, during a limited transition period.

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RÉSUMÉ

Revue des principes fondamentaux du traitement de l'empyème aigu et des causes de l'empyème chronique. Revue des techniques chirurgicales et discussion de celles-ci. Il ressort de l'expérience de la guerre que la méthode de Fowler-Delorme est remise à la page et que la décortication de la plèvre est possible et même indiquées si l'opération est faite assez tôt après le début de l'empyème. L'usage de la pénicilline a encore facilité les choses et il est rare de voir aujourd'hui les empyèmes aigus après une pneumonie. Le danger de retarder la décision de drainer est toujours aussi grand et si l'on choisit de faire le décortication il faut procéder assez tôt.

JEAN SAUCIER

The evaluation of penicillin in the treatment of patients with syphilis is still going on and must continue for several years more before concrete deductions may be made as to its actual value. Penicillin has the following advantages: it produces few reactions and it can be given in a short period of time. The need for hospitalization for a week or ten days and injections given at two or three hour intervals are its disadvantages. It may be that penicillin in beeswax and peanut oil will overcome these objections.—P. A. O'Leary and R. R. Kierland, *J. Am. M. Ass.*, **132**: 428, 1946.

SPLENOSIS

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SPLENECTOMY is the recognized treatment for an increasing number of diseases which formerly belonged in the province of medicine, as well as being imperative in rupture of the spleen. Curtis and Movitz[1] reported a series of 178 splenectomies covering a list of 21 diseases for which splenectomy was indicated. They found congenital hæmolytic icterus to be the disease in which it was most commonly indicated—53 cases or 29.7% in their series of 178 cases. The next most common indication was primary thrombocytopenic purpura, 33 cases or 18.5%.

The spleen is coming more and more into the field of the ductless glands. Hypersplenism or an increase in splenic secretions is being looked upon as a possible cause for the destruction of all or certain elements of the blood, such as that found in thrombocytopenic purpura where only the platelets of the blood are affected, and again in congenital hæmolytic icterus, where a marked destruction of the erythrocytes goes on, due to an increased fragility of the cells. The increased pigments in the blood and tissues from the broken-down erythrocytes which must be excreted by the liver results in a high incidence of gallstones of the bile pigment type. In a series of 118 cases reported by Pemberton[13] "conclusive evidence of disease of the gall bladder, with or without stones occurred as a secondary complication in 81 cases (68.6%)".

There is nothing more convincing in surgical therapy that the spleen is the causative factor in these two blood diseases than the dramatic and usually lasting improvement that follows removal of an enlarged and obviously diseased spleen. One boy from whom I removed the spleen at the age of 17, for congenital hæmolytic icterus of the familial type—his father and one sister had splenomegalia also—has been four years in the army during the recent war. It is now eighteen years after splenectomy, and there has been no recurrence of his jaundice or anæmia. There are, however, cases that recur after a period of cure or marked improvement following splenectomy. If recurrence occurs, McLaughlin, Sharpe and Cunningham[2] concluded that: (1) the original diagnosis was in-

correct; (2) overlooked splenic tissue had become active; or that (3) hæmolymph nodes had hypertrophied and assumed excessive hæmolytic activity.

Curtis and Movitz[1] believe the recurrence to be due to overlooked accessory splenic tissue. They report a case of recurrence in a patient in which an accessory spleen was observed but not removed at the time of splenectomy. They report another case of recurrence in which the patient died and the accessory spleen was found at necropsy. But their most convincing case was a case of recurrence relieved by the removal of an accessory spleen. The incidence of accessory spleens varies according to age. They are much more common in infancy and childhood and tend to decrease with advancing age, from some form of involutional atrophy. Adami and Nicholls[3] report an incidence of 11% in all their autopsies. The incidence is also greater in patients with splenic disease. Curtis and Movitz[1] report 56 cases, or an incidence of 31.4% of accessory spleens found in a series of 178 cases of splenic disease. Maingot[4] reported an incidence of 44.4% of accessory spleens found in a series of 18 cases where the spleen was removed for primary thrombocytopenic purpura. Vaughn[5] reported a 17% recurrence of primary thrombocytopenic purpura following a period of relief after splenectomy in a series of 303 cases. Curtis and White[6] think that this 17% recurrence corresponds closely enough with Adami and Nicholls 11% incidence of accessory spleens to attribute the recurrence to the accessory spleen.

True accessory spleens are only found in areas where splenic tissue developmentally arises, not on the parietal peritoneum or ventral mesogastrial layers, and are limited in number, there being rarely more than ten. There is, however, another condition in which multiple pieces of splenic tissue are found attached and growing throughout the whole peritoneal cavity, on parietal as well as visceral peritoneum, in the pelvis, on the diaphragm, omentum and dome of the liver. In one case reported by Shaw and Shafi[7] a portion of splenic tissue was found growing in the left thoracic cavity opposite the eighth dorsal vertebra, together with numerous other small splenic implants in the peritoneal cavity of the same patient (Fig. 1). Albrecht in 1896 (quoted by Curtis and Movitz[1]) was the first to report a case of this kind; there were as many as four hundred small accessory spleens in the patient, and a similar case by Orth was cited. Since then there have been 15 similar observations reported, according to Waugh,[12] 4 of which are in the American literature. Hamrick and Buch[8] give a synopsis of 13 of these cases and since then there have been two others reported, one by Waugh.

These multiple splenules are not considered in the same category as the usual accessory spleen. They have been found either during a subsequent laparotomy or at autopsy, in patients who have had a splenectomy for traumatic rupture or in patients who gave a history of an abdominal injury in the region of the spleen.

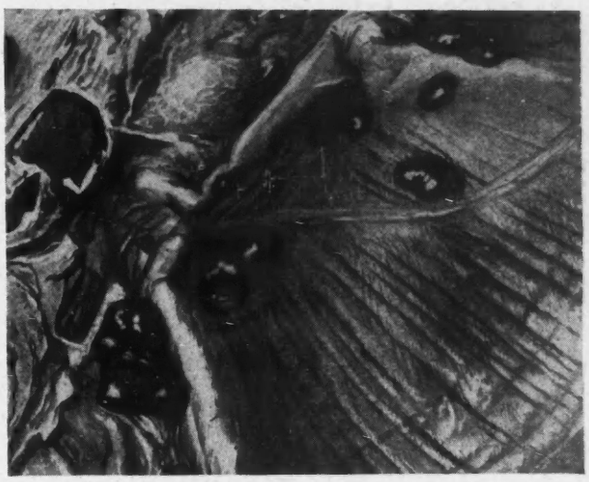

Fig. 1.—Part of left vault of diaphragm showing a number of splenic transplants. Natural size.
(From Shaw and Shafi's article.)

It has been shown experimentally that splenic tissue may be implanted in the peritoneum and readily survives transplantation. Von Stubenrauch (quoted by Buchbinder and Lipkoff[9]) removed the spleen in several dogs, crushed the pulp and "seeded" these throughout the peritoneal cavity. On sacrificing the dogs from one to three months later, he was able to demonstrate the same picture he described in man. Marine and Manley[10] in 1920 and Perla[11] in 1936 showed the readiness with which autoplastic splenic transplants grow in rabbits and albino rats although their transplants were into the abdominal wall and not the peritoneum. Buchbinder and Lipkoff[9] think Foltin in 1911 to be the first to suggest that these multiple splenules were "seeded" throughout the peritoneal cavity in man by the blood which carried splenic pulp cells to all areas of the abdominal cavity at the time of the ruptured spleen.

Buchbinder and Lipkoff originated the term "splenosis".

So far I have been unable to find any case reported in which widely disseminated splenic nodules were found following splenectomy for non-traumatic disease of the spleen. Shaw and Shafi express the opinion that the removal of diseased spleens apparently is rarely, if ever, followed by implants, in spite of occasional tearing and its associated hæmorrhage during splenectomy. This same opinion is held by several other authors including Waugh[12] and Hamrick and Bush[8] who also make the statement that "as yet no symptoms have been known to result from these splenic implants". The following case would appear to be the first recorded case in which autoplastic transplants of splenic tissue occurred in the abdomen following splenectomy for a non-traumatic condition and also in which these transplants have caused a recurrence of the disease for which splenectomy had been performed, namely congenital hæmolytic icterus.

Case Report

Mrs. H. This patient, a married woman of 23 years, came under my care in September, 1940. There was nothing of significance in the family history other than that her mother and one sister had gallstones. This girl had never been strong, had "weak spells" and her complexion was always sallow and muddy. At the age of 18 years, her doctor told her she had gallstones, and her history for the five years preceding admission to hospital was a clear cut history of dyspepsia due to cholecystitis. On admission she was five months' pregnant, deeply jaundiced, the jaundice having had its onset ten days previously following a severe attack of upper abdominal pain. The laboratory data were as follows: red blood cells 3,110,000; white blood cells 15,000; Hg. 53%; icterus index 41; van den Bergh, delayed direct reaction 7.2; the urine showed bile 3 plus and bile salts 3 plus; temperature, pulse, and respiration were normal.

She complained of pain under the right costal margin and was extremely tender to touch in this area. The diagnosis of acute cholecystitis was obvious. After vitamin K, transfusions of blood, glucose and saline therapy, she was operated upon under spinal anæsthesia. At operation the gall bladder was found to be acutely inflamed and full of stones. The gall bladder and contents were removed. Five black, sharp, jaggy stones were found in the common bile duct, proximal to a stricture in the common bile duct, situated between the entrance of the cystic duct and the bifurcation of the hepatic duct. These stones were removed, the stricture was dilated and a "T" tube drainage established with the lower limb of the tube through the stricture. Her convalescence was very stormy; drainage was poor through the "T" tube. The jaundice cleared slowly. However, she carried on and on December 1, 1940 was delivered of a normal, healthy child, three months after cholecystectomy. She gained strength very slowly. The jaundice never completely cleared and in February, 1941, it began to deepen and continued to do so until April, at which time she was re-admitted to hospital, deeply jaundiced. The laboratory findings were: red blood cells 3,310,000; white blood cells 15,650; Hg. 54%; icterus index 50; van den Bergh, qualitative prompt direct; quantitative 7.2 unit.

It was obvious that the stricture had recurred. A second operation was performed at which the stricture was excised and the gap bridged with a rubber tube. Convalescence was satisfactory, the jaundice disappeared slowly, but she remained pale and sallow. Following this she led a fairly normal life for about one and one-half years, then began to have "weak spells" again. The jaundice returned, unaccompanied by pain or indigestion and gradually deepened until October, 1942. She was re-admitted to hospital one and one-half years after the second operation. Her blood studies showed: red blood cells 3,215,000; white blood cells 31,950; Hg. 73%; icterus index 30.

On this occasion she was found to have a greatly enlarged spleen and the diagnosis of congenital hæmolytic icterus was made. After being given vitamins, blood and parenteral fluids, a splenectomy was done on October 16. The spleen was greatly enlarged weighing 479 gm. and was found to be attached by dense adhesions to the stomach, diaphragm, colon and parietal peritoneum. The operation was difficult and very bloody due to tearing of the capsule.

Her convalescence was rapid and the jaundice cleared very quickly. Her colour was better than it had ever been in her life and she enjoyed better health than ever before, until September, 1945, when she had a few crampy pains in the upper abdomen followed by a slight tinge of jaundice, which soon cleared after she passed the rubber catheter by bowel four and one-half years after it had been inserted. She was then as well as formerly until early 1946, when she became pregnant and her former attacks of fatigue reappeared, her complexion became sallow and the jaundice soon reappeared. She was re-admitted to hospital in July, 1946, eight months' pregnant, showing: red blood cells 2,900,000; white blood cells 32,450; Hg. 54%; icterus index 41.

She was suffering a great deal of abdominal pain which was thought to be caused by the increasing size of the uterus stretching an abdomen which was limited in size by numerous adhesions. After blood transfusions, vitamins and fluids, a Cæsarean section was done on July 5. When the abdomen was opened, numerous spleen-like masses were found scattered throughout the whole abdomen. Their true significance was not realized at the time, although I made the remark that they looked like small spleens. Six of these tumours were removed and sent to the pathologist and he confirmed the diagnosis of splenic tissue. No attempt was made to count them, but there must have been over one hundred. They were in the pelvis, on the parietal peritoneum, the surface of the uterus, and very numerous on the omentum, ranging in size from a pea to that of a plum, and the colour of a normal spleen.

Convalescence was slow, but she gradually improved and left the hospital on July 15. She returned in September for a check-up. She then looked well, her complexion was clear, although still slightly anæmic: Hg. 72. Otherwise her blood picture and laboratory tests were normal.

Summary and Conclusions

A case of splenosis is reported, in which "seeding" occurred after splenectomy for non-traumatic reasons.

The case is the first to be reported in which the splenic transplants showed function.

The surgical technique for splenectomy for either traumatic or non-traumatic reasons should be designed to completely remove all blood from the abdominal cavity and the abdominal wall incision should also be protected from splenic blood to prevent implants.

A recurrence of congenital hæmolytic icterus following splenectomy may be caused by splenosis.

I wish to acknowledge the splendid assistance given me by our pathologist, Dr. J. B. McKay, in the laboratory tests necessary to diagnose the several phases of this case.

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NEW FACTORS IN THE ETIOLOGY OF OBLITERATIVE ARTERIAL DISEASE*

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THIS brief report has been prepared in an attempt to shed some further light on the etiology of obliterative arterial lesions of the legs. The subject material is taken from 25 cases recently studied in the Vascular Service of the Royal Victoria Hospital and certain conclusions are drawn from the clinical and laboratory investigations, and also from the fact that in every case a specimen of artery for pathological examination was obtained from one of the leg arteries.

The diagnosis of obliterative arterial disease of the lower limb is not too difficult to make providing one keeps the condition in mind and spends a few minutes in the examination of the feet and legs. A true history of intermittent claudication or ischæmic neuritis, and the absence of pulsations in the dorsalis pedis, posterior tibial and popliteal arteries are easily determined. The presence of ischæmic changes in the foot with blanching on elevation and rubor on dependency will corroborate the findings. However, the determination of the type of obliterative disease is a much more difficult matter.

In following the present day literature on this subject there appear to be only two causes of chronic ischæmia of the extremities. These are Buerger's disease and arteriosclerosis. The differential diagnosis between Buerger's and an early case of arteriosclerosis has been most difficult to make but, in brief, it appears that in the past the diagnosis of Buerger's disease was mainly made by excluding any evidence of arteriosclerosis in the patient. This diagnosis was aided by such additional evidence as the youth of the patient, his being of the Jewish race, with a history of heavy smoking, and perhaps of a migrating phlebitis. Using such criteria therefore, the majority of cases of obliterative vascular disease up to the age of fifty were diagnosed as Buerger's. Such was the situation preoperatively in 19 of our 25 cases.

It is the purpose of this paper to present some evidence that the picture is not quite so simple as this; that Buerger's disease is relatively rare; and to describe a group comprising the majority of our cases, showing a picture which is neither Buerger's disease nor arteriosclerosis as we now define it.

METHODS AND RESULTS

In the cases studied, an investigative routine was carried out and consisted of a hæmogram, electrocardiogram and cardiac examination, blood Wassermann, x-ray of the arteries of the pelvis for calcification, examination of the fundi for evidence of arteriosclerosis, oscillometric readings of the leg arteries and skin temperature readings before and after lumbar sympathetic procaine block. More recently we have used the new drug tetra ethyl ammonium chloride to check the results of the sympathetic block. This drug causes a paralysis of the autonomic nervous system at the ganglionic synapses for varying periods of time depending on whether it is given intravenously or intramuscularly. The results in skin temperature readings have closely paralleled those following lumbar sympathetic block.

All cases had pathological examination of a leg artery taken either from an amputation specimen or from biopsy of the dorsalis pedis artery at the time of sympathectomy.

Six of the 25 cases showed evidence of arteriosclerosis in the fundi or on x-ray of the

* From the Surgical Service of the Royal Victoria Hospital and McGill University. Presented before the Royal College of Surgeons of Canada in Ottawa, November 16, 1946.

pelvic arteries and usually there were suggestive findings also in the cardiogram. No diabetic is included. All of these six showed rises of skin temperature over two degrees C. in the foot following lumbar sympathetic procaine block and were consequently treated by lumbar sympathectomy. These findings indicate, contrary to previous belief, that the majority of early arteriosclerotics are capable of considerable vasodilatation of their collateral system.

In the remaining 19 cases a tentative diagnosis of Buerger's disease, active or quiescent, was indicated according to the existing criteria. However, on pathological examination only four were proved to be Buerger's, these all requiring amputation, and being the only amputations in this series (Figs. 1 and 2).

affected side, simulating an aneurysm, and the plaques were demonstrated by palpation at the time of sympathectomy.

This leaves 11 cases with no clinical or laboratory evidence of arteriosclerosis, who on examination of a biopsy section of the dorsalis pedis artery showed no evidence of Buerger's disease. I would like to discuss this group in some detail as I believe their significance has hitherto not been appreciated.

These were all males in the middle and older age groups, the youngest being 43 and the oldest 62. Their complaints were chiefly intermittent claudication, which had been present and gradually increasing over a period of one to two years. All were moderate to heavy smokers. Examination revealed one leg involved in 5 and bilateral involvement in 6.

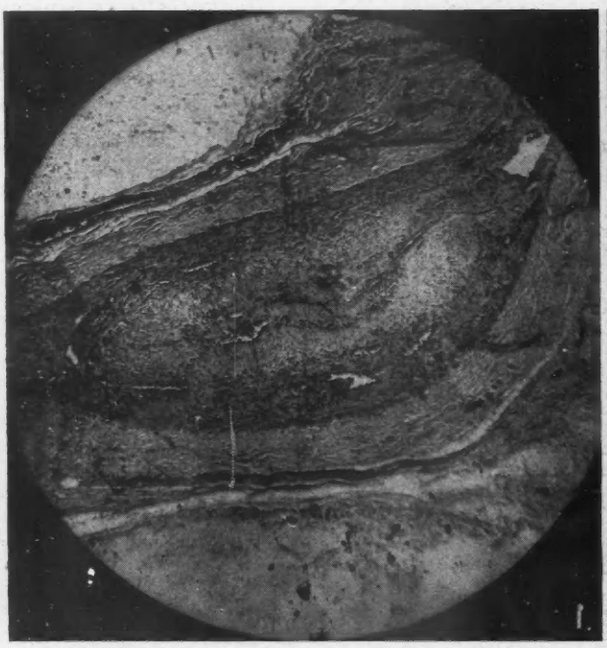

Fig. 1.—Section of dorsalis pedis artery in a case of Buerger's disease showing the well organized thrombus blocking the lumen, one area of recanalization, and the round cell infiltration of the arterial wall and surrounding tissue. **Fig. 2.**—Low power view of a case of Buerger's disease showing the typical changes involving not only the artery but, as is usual, the entire neurovascular bundle.

Four cases were found to be due to miscellaneous causes, one being a young man with intermittent claudication subsequent to a bland thrombosis of the arterial system of one leg from the mid-femoral downwards following a fracture of the ankle. The second was a similar case, but subsequent to an acute attack of scarlet fever. Their pathological picture was almost identical. The other two showed arterial ischæmia in one leg subsequent to narrowing of the common iliac artery from an undetected atheromatous plaque. Both had loud systolic bruits heard over the common femoral on the

The ischæmic changes in the foot were minimal, but pulsations in the dorsalis pedis, posterior tibial and popliteal arteries were absent and, in one case, in the femoral. Oscillometric readings were greatly diminished in the involved extremities. The special investigations above mentioned were otherwise negative. Intradermal nicotine sensitivity tests were inconclusive. All showed a moderate to good response in the improvement of skin temperature readings following lumbar sympathetic procaine block and consequently all were treated by lumbar sympathectomy with a co-

incident biopsy of the dorsalis pedis artery. Examples are shown in Figs. 3 and 4.

The comparison of these pathological specimens with those shown in Figs. 1 and 2 definitely rules out a diagnosis of Buerger's. The same can be said for arteriosclerosis of the usual medial or intimal type. There is no inflammatory or thrombotic process, and all one can say is that some evidence of chronic degenerative change is present.

It is probable that this picture is not a separate disease entity but one of the earliest changes in the development of an arteriosclerosis. It is difficult to be certain why, with such early changes, arterial obliteration and ischæmia should result when in others with fully developed arteriosclerosis no such condition occurs. One possibility may be that this picture in the dorsalis pedis artery may be due to a blockage by an unrecognized thrombosis higher in the vessel. Examination of the uterine arteries shortly after childbirth, where the flow in these arteries has been suddenly reduced after delivery of the child, will show much the same pathological picture.

It is our belief at present, but based on very little evidence, except that this group is placed toward the latter part of life, that these 11 cases showing the chronic degenerative changes on biopsy are due to local areas of thrombosis in a main limb artery probably on the basis of an undetected atheroma.

SUMMARY

As a result of this study, we have come to the belief that Buerger's disease is much less common than is generally believed, that it is a generalized progressive disease responding only briefly to the present methods of treatment, including sympathectomy, and that leg amputation is a very frequent sequel. On the other hand we believe that the group showing the chronic degenerative process on biopsy has a much better prognosis due to the slowness of the progression of the disease. They also show long lasting improvement following lumbar sympathectomy.

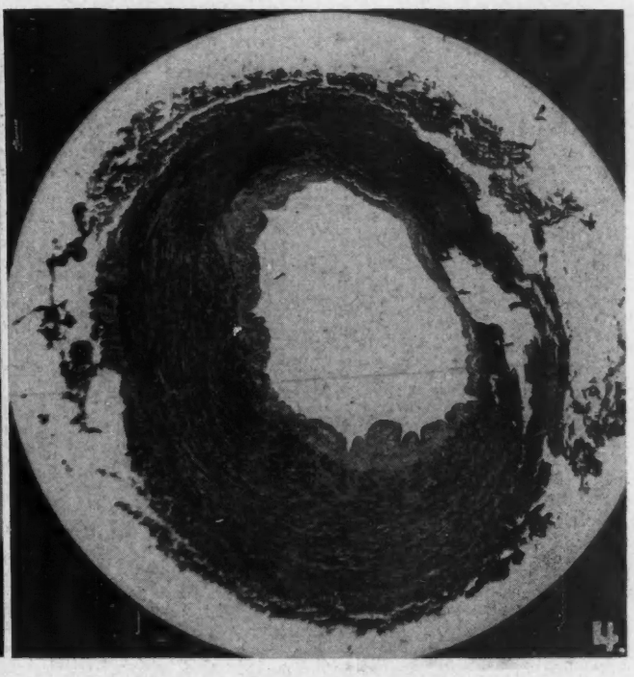

Fig. 3.—Section of dorsalis pedis artery showing evidence of chronic degenerative changes consisting of a markedly thickened intima, fibrous replacement in the medial coat but no evidence of inflammatory or thrombotic changes. **Fig. 4.**—Tri-chrome stain of a similar case indicating the degree of fibrous tissue replacement of the muscular medial coat. No evidence of calcification or atheromatous changes.

It is our opinion that the many glowing reports previously published of the good results of sympathectomy and other treatments in Buerger's disease are incorrect, inasmuch as what is being reported as Buerger's is not necessarily proved.

And finally we feel that a correct etiological diagnosis of arterial occlusive disease of the legs is most difficult, especially in the young and middle-aged group, but that biopsy of one of the main arteries, preferably at the time of sympathectomy, will give the most information possible.

THE SURGERY OF HEART DISEASE*

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THE carrying out of surgical operations on patients with heart disease has traditionally been considered a very serious matter. How much more serious then must the operation be if it is undertaken because of heart disease, and even performed on the heart itself? The fact is that in actual practice under present-day conditions, and provided certain rules are observed, the risk is relatively small; it becomes less and less each year as more satisfactory methods are developed for the control of harmful reflexes, and with the growth of surgical experience and improvement in techniques.

Table I comprises a list of the diseases of the heart and great vessels for which surgery has been attempted, and the operations devised for them. Many of these operations are not actual cardiac surgery: those done in the congenital lesions are for instance carried out entirely on the blood-vessels, and most of the operations for the relief of pain are neurosurgical.

TABLE I.

OPERATIONS FOR THE TREATMENT OF DISEASES OF THE HEART AND GREAT VESSELS

1. Pericardial Disease:
   - *a.* Drainage of pyogenic infections.
   - *b.* Cardiolysis (Brauer).
   - *c.* Pericardial resection (Delorme).
2. Congenital Abnormalities:
   - *a.* Ligation of patent ductus arteriosus (Gross).
   - *b.* Subclavian to pulmonary artery anastomosis (Blalock).
   - *c.* Excision of coarctation of aorta (Crafoord).
3. Coronary Arteriosclerosis:
   - *a.* Interruption of nervous pathways:
     - i. Cervical ganglionectomy (Jonnesco).
     - ii. Stellate ganglionectomy (Lariche).
     - iii. Injection (Mandl) or excision (White) upper dorsal sympathetic chain.
     - iv. Posterior rhizotomy (Singer).
     - v. Anterior rhizotomy (Raney), with section of posterior roots (Cone).
     - vi. Pericoronary neurectomy (Fauteux).
   - *b.* Introduction of extracardiac collateral vessels:
     - i. Pectoral muscle graft (Beck).
     - ii. Omental graft (O'Shaughnessy).
     - iii. Formation pericardial adhesions (Beck).
   - *c.* Ligation of great cardiac vein (Fauteux).
4. Congestive Failure:
   - *a.* Total thyroidectomy (Blumgart).

I have not included surgery of the valves in the list. The operation of valvulotomy for mitral stenosis has never had any success, and so far as I know has been entirely abandoned. The removal of enough of the rigid valve to cause a free mitral regurgitation is physiologically unsound, and in the rare clinical cases where this lesion does occur through ulceration of the valve a tremendous strain is placed on the left auricle as well as on the left ventricle. Mitral valve repair as carried out experimentally by Murray, Wilkinson, and MacKenzie[15] has as yet no application in man. It is possible that some day somebody may devise an artificial valve, perhaps of metal, which could be seated in the aorta to relieve severe aortic regurgitation; a prerequisite would of course be the development of some means of sidetracking the bloodflow during the operation.

PERICARDIAL DISEASE

It is unnecessary to stress the importance of surgical drainage of the pericardium whenever pyogenic infections are diagnosed. The prognosis in these conditions has been greatly improved by the use of sulfonamides and penicillin: irrigation of the infected cavity with penicillin may be a very important part of the procedure.

The effectiveness of pericardial resection in relieving the congestive failure caused by constrictive pericarditis is now widely recognized and requires little comment. The chief points in diagnosis are a rise in venous pressure, obstruction to the portal circulation resulting in liver enlargement and ascites, and impairment of cardiac mobility and of excursion of pulsation. Calcification of the pericardium is not found in all cases, nor even in the majority: it should be recalled that extensive calcification is compatible with freedom from disability, and so does not of itself call for operative interference. A point of the highest importance for operative success is the choosing of an experienced surgeon.

Brauer's operation consists in removal of the bony thorax overlying the heart. It was earlier thought that the mediastino-pericardial adhesions of obliterative pericarditis could, through bringing about retraction of the chest wall during systole, result in cardiac enlargement, and the operation was done to correct this. Later realization that enlargement in these cases is nearly always caused rather by coincident valvular disease[18] has been perhaps the main reason

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why it is now seldom performed. Good results that are occasionally reported are probably attributable to actual decompression of a greatly enlarged heart, from whatever cause. There seems little doubt that the operation has a useful place in relieving the dysphagia which sometimes occurs in mitral stenosis when the left auricle is tremendously enlarged.[16]

CONGENITAL ANOMALIES

A new field in vascular surgery was opened up with the first successful ligation of a patent ductus arteriosus by Gross[13] in 1939. Thenceforward the differential diagnosis of congenital heart disease became of necessity more than a purely academic problem: its importance was accentuated later when Taussig conceived her brilliant idea of short-circuiting systemic blood to the lungs in certain cyanotic lesions, and Blalock worked out an operative technique.[2] New methods of diagnosis have been called into play. Important information can for instance be obtained from angiocardiography, the outlining of the heart chambers by intravenous injection of opaque dyes.[5, 24] We are finding intracardiac catheterization of great value; by it variations in the oxygen tension of the blood in the different chambers can be determined, and the position of shunts thereby recognized (see Fig. 1).

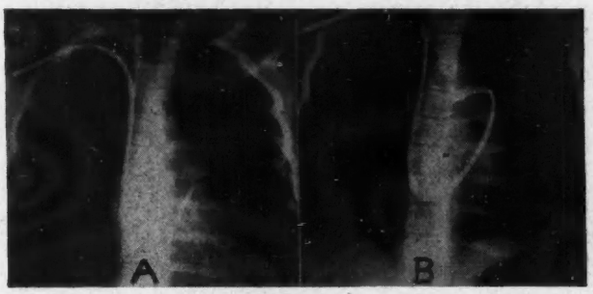

Fig. 1.—Intracardiac catheterization in a boy aged 11. In A catheter tip is in right ventricle, and in B it is in right pulmonary artery. Higher oxygen content of blood from position B indicates diagnosis of patent ductus arteriosus, later confirmed at operation. (Courtesy of Dr. Arnold Johnson).

Ligation of a patent ductus that is not infected is now, when done by a competent surgeon, a relatively safe procedure. Shapiro[23] found only a 4% mortality in 505 such cases which he recently collected; Dudley Ross,[22] at the Children's Memorial Hospital in Montreal has had no deaths in his series of 30. Although statistics like this, and the knowledge that a high percentage of patients eventually contract subacute bacterial endarteritis, tend to make one consider the advisability of operating in every case, nevertheless the operative risk is still such that it is at least doubtful whether it should be done if there is a complete lack of disability. But any abnormal dyspnœa on exertion, and the presence of physical underdevelopment, are to my mind definite indications. Because the ductus may sometimes close spontaneously, infants, unless they have obvious signs of failure, should be left alone until childhood. In adults rigidity and calcification of the ductus make the operation more difficult.

The prominent pulmonary artery usually found in this congenital anomaly is undoubtedly an indication of strain on that vessel, and it may well be that as the operative mortality falls, the presence of this isolated sign will be considered grounds for interference.

Subacute bacterial endarteritis engrafted on a patent ductus has until recently been considered a positive indication for operation, and the results in those who survive are excellent. But the mortality rate in these infected cases is so high—28% in Shapiro's[23] series of 121—and the efficacy of penicillin therapy in most other subacute bacterial endocarditis such, that this latter treatment should probably be given a thorough trial by itself, before operation is decided on. I say this however, without any personal experience.

The Blalock operation is designed for the treatment of cyanosis when this is caused through inability of the blood to reach the lungs in adequate amounts. The pulmonary stenosis in Fallot's tetrology is of course the prototype for the operation, which consists in anastomosing one of the early branches of the aorta, preferably the subclavian artery, to the pulmonary artery.* An artificial patent ductus is thus created, which is in itself a defect. Because of this, and of the fact that the communication between the two ventricles must necessarily remain, the operation can never produce a normally-functioning circulation. In spite of the still fairly high operative mortality the results in those that survive are so satisfactory that the operation is thoroughly justified. As yet, only those patients who are considerably handicapped should be operated

* It was logical to foresee that one of the first technical improvements to be made in Blalock's operation would be to create a direct communication between the aorta and pulmonary artery, and this has recently been done.[19]

on: later, as greater experience is accumulated, there is no doubt that the scope of the operation will be extended to include the less severe cases.

Coarctation of the aorta can be corrected by excision of the narrowed or obliterated area, with anastomosis of the two severed ends.[6] This too is a serious major operation, and should only be undertaken when the degree of hypertension present is likely to lead to heart failure or a vascular accident.

CORONARY DISEASE

The treatment of coronary disease by surgery has evoked a considerable variety of approach. The result is a rather large number of operations, which at the same time testifies both to the lack of unqualified success by any one of them, and to the continued search that is being made for better methods. The operations fall into two large groups, that in which the attack is on the nervous pathways to and from the heart, and that in which it is directly on the myocardial circulation itself.

Neurosurgical operations.—Most of these have been designed to relieve the pain through interruption of the sensory pathways from the heart (see Fig. 2). It is possible, but not proved, that the alteration of vasomotor mechanisms may also play a part. The pain pathways are located only in the sympathetic nerves, and not in the vagus. When Jonnesco in 1920 resected the cervical chain for angina pectoris, he did so in the belief that all pain sensations reached the sensorium by way of the cervical cardiac nerves. The fact that the cervical sympathetic connections with the spinal cord are by way of the upper thoracic ganglia made it apparent that stellate ganglion resection would interrupt the pain pathways just as effectively as Jonnesco's operation. But in somewhat less than half the cases in which these two operations were performed they failed to relieve the pain; the reason for this only became apparent when it was discovered in 1927 that the cardiac plexuses are directly connected with the upper four or five thoracic sympathetic ganglia by thoracic cardiac nerves. Anginal pain can be effectively relieved by resection or alcohol injection of these ganglia.[27] This same result can be achieved by interrupting the sensory fibres as they pass through the dorsal roots (dorsal rhizotomy).

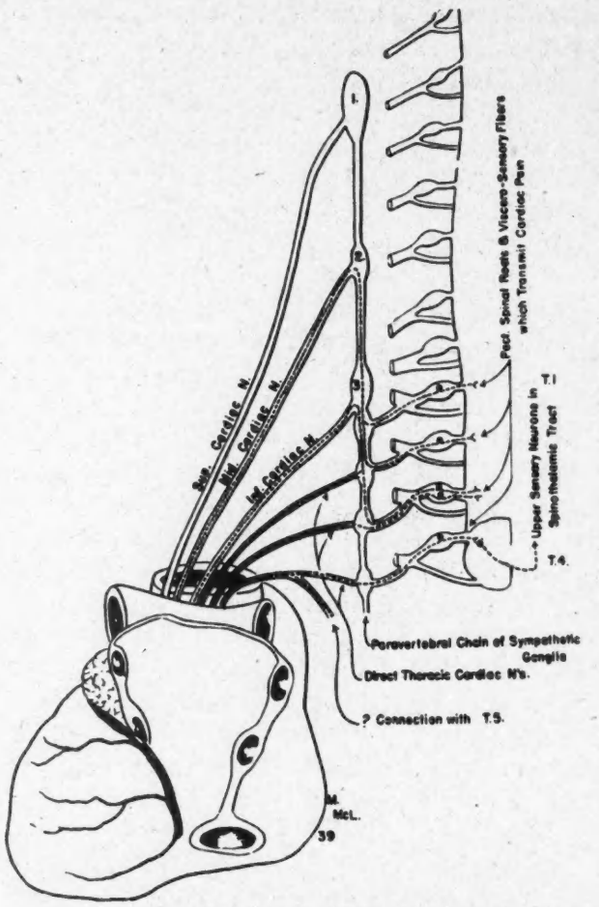

Fig. 2.—The pain pathways from the heart. (After J. C. White. Courtesy of the Association for Research in Nervous and Mental Disease).

In the belief that some of the success of these nerve ablation operations is due to the removal of sympathetic vasoconstrictor impulses to the coronary vessels Raney[21] interrupted the efferent fibres by performing anterior rhizotomy. Cone[7] has modified this operation by severing at the same time the posterior roots, thus removing the pain pathways. The advantage of this anterior root section is that it is preganglionic; unfortunately there is still some uncertainty as to whether the sympathetic supply to the heart is constrictor or dilator. Another operation which is effective at a different site is Fauteux's[9] pericoronary neurectomy; here the plexus itself, including of course sympathetic and vagus fibres, is destroyed at the root of the aorta and pulmonary artery. This neurectomy is only part of a larger operation and will be discussed later.

All these operations are still being done. Resection of the whole cervical chain has been pretty well abandoned in favour of stellate ganglionectomy which is fairly popular in

Europe. Its simplicity is recognized, but the high percentage of failures makes it difficult to recommend it. Alcohol injection of the upper dorsal sympathetic chain is not a serious operation, but demands considerable technical skill. Its great drawback is the postoperative neuritic pain which develops in the intercostal nerves. The seriousness of this may be appreciated by mentioning the experience of one intelligent patient who remarked that when he had his angina he was afraid that he might die from it, but when he had his neuritis he was afraid that he might not die! Operative removal of the dorsal chain is not followed by neuritis; it is on the other hand an extensive operation, and for this reason division of the posterior roots, which can be done more easily, and in which there is less shock, is coming to be preferred by neurosurgeons.

Very few cardiologists are, I think, eager to recommend any operation that merely interrupts the pain pathways, but if such a decision is made, and a neurosurgeon is not available, alcohol injection of the upper thoracic chain is the operation of choice. The criticism that these operations remove the warning signal and are therefore dangerous, is not valid, as minor sensations still replace the major pain in nearly every case.

Development of extra-cardiac blood supply.—The earliest experimental work which aimed at establishing an extraneous collateral blood supply in coronary disease was that of Beck in 1932. Basing his work on the previous observation that blood vessels had been seen to pass between the thoracic wall and the heart in patients with obliterative pericarditis, he endeavoured to bring new vessels to the heart by means of grafts.' For these he made use of fibrous pericardium, pericardial fat, omentum, and skeletal muscle from the chest wall, finally settling on the latter tissue for his first human operations. Thirty-seven patients were treated by this procedure, with an operative mortality of 38%. Of the 23 patients who survived, 14 are described by Feil[11] as having an excellent result, and five more a good result. It seems obvious that an operation with such a high mortality as this will not have a wide appeal. Beck[1] himself now says that his aim can be best achieved by his later operation of scarification of the parietal pericardium with consequent application of asbestos powder. A modification of this is the insufflation of powdered talc into the pericardial cavity which has been done by Thompson and Raisbeck.[25] Long-term results in these induced pericarditis cases are awaited with interest.

Shortly after Beck began his grafting experiments, O'Shaughnessy[17] independently began using omental grafts brought up through the diaphragm and sutured to the heart. Before his death early in the war he had claimed satisfactory results in most of his human cases, but the operation never became popular, and, so far as I know, is not now being done.

Several important criticisms of the pericardial graft method have appeared, notably those of Burchell[3] in which he states that he was unable to show that any vascular channels in pericardial adhesions in his dogs were functionally worth while. It does not follow however that one should apply conclusions drawn from negative results in animal experiments directly to man. When definite areas of localized ischæmia are present in the human heart, the pressure gradient could easily be such that the new vessels produced by pericardial inflammation would invade the ischæmic areas and become effective collaterals. That this actually takes place when the ischæmic area involves the external surface of the heart seems to have been demonstrated; its effectiveness when the ischæmic area lies deeper is at least doubtful.

Ligation of the great cardiac vein.—An entirely different approach to the problem of improving the myocardial circulation was used by Fauteux. It had been demonstrated by Oppel in 1913 that venous ligation in a limb was a valuable procedure in dealing with arterial disease or injury. Furthermore, Louis Gross had shown that occlusion of the coronary sinus appeared to compensate in some way for later ligation of a coronary artery. Fauteux satisfactorily demonstrated that ligation of the great cardiac vein would protect his experimental dogs from myocardial infarction when the descending ramus of the left coronary artery was later resected. The decision followed to apply these results to the treatment of myocardial ischæmia in man, and subsequently he operated in Montreal on a series of ten patients. Nine of them were suffering from severe angina pectoris, and the other had had several attacks of coronary occlusion. The first case was reported by Fauteux and myself[10] in 1941, and the remainder by Fauteux[9] in 1946.

The non-anginal patient died postoperatively of tension pneumothorax, the only operative death in the series. The others were entirely freed from their anginal pain, except one, and he was much improved. Two patients died since operation, one three months later, and one two and a half years later. The remaining seven are alive, and working at their old occupations, now from four to six years after operation.

Some light has been shed on the physiological mechanisms involved in Fauteux's operation by the work of Gregg and his associates[12] in Wiggers' laboratory. They found that when the coronary sinus is abruptly occluded the pressure in it rises from low values to figures which may even exceed during systole the aortic systolic pressure, and during diastole may still be from 20 to 40 mm. Hg. A rise in pressure of this order also occurs in the peripheral arterial bed if now a coronary artery is ligated; upon severing this artery distal to the ligation the retrograde flow from the peripheral end is seen to rise from a control maximum of one c.c. per minute to as high as 40 c.c. This blood always shows a very much lower oxygen content than ordinary venous blood. Their conclusion was that under those experimental conditions the retrograde flow afforded adequate nourishment to the myocardium which had been deprived of its normal supply. When the great cardiac vein instead of the coronary sinus was occluded, the same changes in circulation occurred, but in much lesser degree.

The rise in pressure in the great vein can be easily seen at operation, but circulatory measurements comparable to those carried out in animals have not been made in the human. Gregg's observation that a decrease in coronary artery inflow occurs when the venous outflow is blocked was regarded by him as an effect deleterious to the heart. If there is any such acute coronary insufficiency during the operation in man we have been unable to detect it with the electrocardiograph; nor has Fauteux found such changes in his experimental dogs.

Some of the newer anatomical discoveries are highly pertinent, especially when they are considered in conjunction with the physiological changes described above. Wearn[26] has shown that the myocardial blood sinusoids are in direct communication with small branches of the coronary arteries by means of vessels ranging in size from 50 to 250 micra. (It will be recalled that capillaries measure only from 8 to 12 micra). That direct arterio-venous anastomoses also exist in the human heart has been known for many years: recently Prinzmetal[20] has demonstrated that glass beads ranging in size from 80 to 170 micra can be recovered from the coronary sinus after their injection into a coronary artery. It is therefore evident that the coronary arterioles, the sinusoids, and the venous system are connected with each other by vessels of large calibre.

The above considerations suggest that after ligation of the vein in the human patient suffering from localized coronary ischæmia the pressure gradient is such that retrograde flow into this ischæmic area is brought about. Provided then that the Thebesian system continues to carry off only its estimated normal 60%[14] of the coronary outflow, considerable benefit to the ischæmic muscle would accrue; this in spite of the fact that the myocardium probably derives some of its oxygen from venous blood. A good deal of pooling in the sinusoidal system must occur as a result of the dilatation of these thin-walled vessels by the rise in venous pressure. This dilatation can persist, and was demonstrated in one case at autopsy two and one-half years after operation (see Fig. 3). It is quite possible that mechanical distension of venous and arterial channels is the most important effect of Fauteux's operation. A likely reason for his high proportion of clinical successes is that the great cardiac vein drains the whole apical region, in which occur most of the damaged areas that give rise to anginal pain.

Fig. 3.—Section of myocardium from patient dying two and one-half years after ligation of great cardiac vein. Note great dilatation of sinusoids and small arterioles. (Courtesy of Dr. Mercier Fauteux).

Fauteux has latterly increased the scope of his operation to include removal of the sympathetic and parasympathetic nerve plexuses at the root of the pulmonary artery and aorta. All impulses reaching and leaving the myocardium by way of the coronary vessels are thereby interrupted, but the nerve supply to the pacemaker is not involved. He terms this procedure pericoronary neurectomy.[9] The object of this neurectomy is to break the reflex arc through the sympathetic and vagus fibres upon which the development of ventricular fibrillation seems to depend, and thus prevent

sudden death should a future coronary accident occur. That the pain pathways are at the same time removed has already been mentioned. It is still an experimental procedure, and its value may be difficult to determine clinically; the pronounced tendency for post-ganglionic sympathetic fibres to regenerate will doubtless be responsible for some failures. During the past two years Fauteux[8] has done the combined operation of great vein ligation and pericoronary neurectomy in ten cases. There were three deaths, two from postoperative thrombophlebitis, and one from coronary occlusion three months later. The other seven are all working, and apart from some tightness in the chest of which two of them complain when they are tired, all have lost their pain.

Fauteux and I[10] in 1941 discussed the selection of patients for his operation, and it does not seem that the criteria then laid down should yet be modified. We feel that the operation should be regarded as a treatment for angina pectoris, at the same time stressing the point that it brings about its results through improving the circulation rather than through mere interruption of pain pathways. We say this because, in spite of its subjectivity, angina still remains the best guide to the severity of local ischæmia. Due attention is of course paid to such corroborative evidence as is given by the electrocardiographic changes after exercise and anoxæmia. We do not feel as yet justified in recommending for operation patients who have recovered from one or more attacks of coronary occlusion but who do not have angina; as experience with the operation grows, it may later seem advisable to include this group.

TOTAL THYROIDECTOMY

Only a word need be said about total thyroidectomy. It has I believe no place now in the treatment of angina pectoris, for which it was once recommended. The low basal metabolic rate necessary to maintain freedom from pain was such that a good many patients had to be kept at the myxœdema level. It may be that the operation has some value in congestive heart failure, provided it can be shown that the patient has enough cardiac reserve to enable him to become free from œdema on rest in bed.[4]

CONCLUSION

Enough has I hope been said in this short review to indicate that the surgery of heart disease, although still young, is in process of growing up. It goes without saying that in this, as in so many other specialties, a close and harmonious liaison must be maintained between physician and surgeon. Both have serious responsibilities: the physician in the proper diagnosis and selection of patients, and the surgeon in improving techniques and in keeping the mortality low. The selection of patients will call for nice judgment. Enthusiasm should be properly held in check; the physician must, in cases referred to him, be prepared to decide against operation probably more often than for it. This will not occur so frequently in the group of congenital lesions and in constrictive pericarditis, where there is no medical alternative, but will happen often in dealing with coronary disease, where a medical regimen has admittedly great possibilities. The preference of the patient himself will often, and I think rightly, be the deciding factor; his illness is all too frequently such that he is more interested in leading a comfortable existence than a long one. If both these benefits can be conferred by operation it is more than justified. The final answer will not be written for a good many years. In the meantime the prospect looks bright.

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SURGICAL MANAGEMENT OF GANGRENOUS BOWEL IN INFANCY*

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RESECTION of gangrenous bowel in infancy has been accompanied by so high a mortality rate as to make it practically prohibitive. In a review of the literature, Dowd[1] in 1913, was able to find only 8 successful cases of resection under one year of age. In 1921, Clubbe,[2] in another review could find a total of only 19 successful cases. Ladd and Gross[3] in 1941 reported a series of 43 resections. Eighteen of these were done by primary anastomosis, 3 successfully, and of the other 25 treated by delayed anastomosis after the method of Mikulicz, 7 recovered, giving an over-all mortality rate of 75%. As late as 1944 Thorek[4] quotes a mortality rate of 80% for resection of gangrenous bowel in infancy.

The late Dr. Edward Archibald, of Montreal, made the statement in 1935 to one of us (D.E.R.) that he had never seen an infant, who had a gangrenous bowel, survive immediate resection and anastomosis. This presentation is based on the successful management of 4 consecutive cases without mortality. The patients were all under the age of 11 months. They all came to hospital in a state of toxicity and dehydration and it was therefore necessary in each case that the electrolytic balance should be established before operation.

A cut-down on the long saphenous vein is the best method for the administration of intravenous fluids, as it not only allows for the transport of the patient to and from the operating room without danger of disturbance of the flow, but also offers the most rapid and certain method of venoclysis. The patients all received whole blood during the various operative procedures. This is of utmost importance, because it not only provides for the loss of whole blood which may occur, but also combats operative shock.

One-half of 1% procaine was used for opening the abdomen and if possible no further anæsthetic was administered. If, however, evisceration or inadequate relaxation of the abdominal wall ensued, then the local agent was supplemented by nitrous oxide or ether.

Stage 1 consisted of delivering or extraperitonealizing the gangrenous bowel (Fig. 1). The bowel, one inch proximal and distal to the gangrenous portion was sutured to the peritoneum by 00000 chromicized catgut on atraumatic needles. The afferent and efferent limbs were also sutured together so as to prevent the egress of the other viscera through the wound (Fig. 2). A hard rubber catheter, consistent with the size of the bowel, was then inserted proximal to the line of demarcation, so as to relieve the obstruction and allow for drainage.

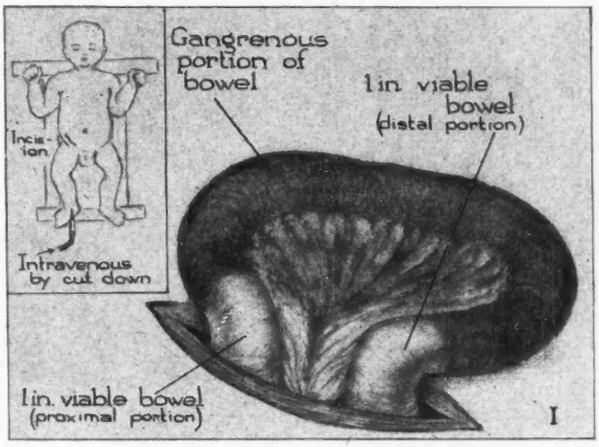

Fig. 1

A vaseline dressing was applied and the patient returned to the ward. Intravenous fluids were then continued and the control of the quantity was based on the known requirements and the clinical condition, which was judged by the elasticity of the skin and the tension of the anterior fontanelle.

Stage 2.—Within a period of twenty-four hours, the gangrenous portion of the bowel was removed by cautery, subsequent to the infiltration of local anæsthetic into that portion of the mesentery subtended by the involved segment. The abdominal wall was covered with aluminum powder, which tends to lessen digestion of the skin around the discharging ileostomy. Whole blood was administered during this procedure.

The general nutrition of an infant with an ileostomy, in spite of the use of adequate intravenous fluids and feedings by mouth, will not remain within normal limits for a prolonged period. It was, therefore, necessary, within a period of two weeks, to proceed with the third

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stage, which is the closing of the ileostomy and the re-establishment of the continuity of the bowel.

Stage 3 consisted of performing an end-to-end anastomosis, subsequent to the freeing of the bowel from the peritoneum, using a continuous suture for the first layer and interrupted sutures for the second (Fig. 2). Since the introduction of sulfonamides, about 30 grains of sulfanilamide micro crystals have been introduced at the site of the anastomosis. The infants were maintained on intravenous fluids, with nothing by mouth for 24 hours. On the second day feedings were commenced, supplemented by intravenous fluids for the assurance of an adequate fluid intake.

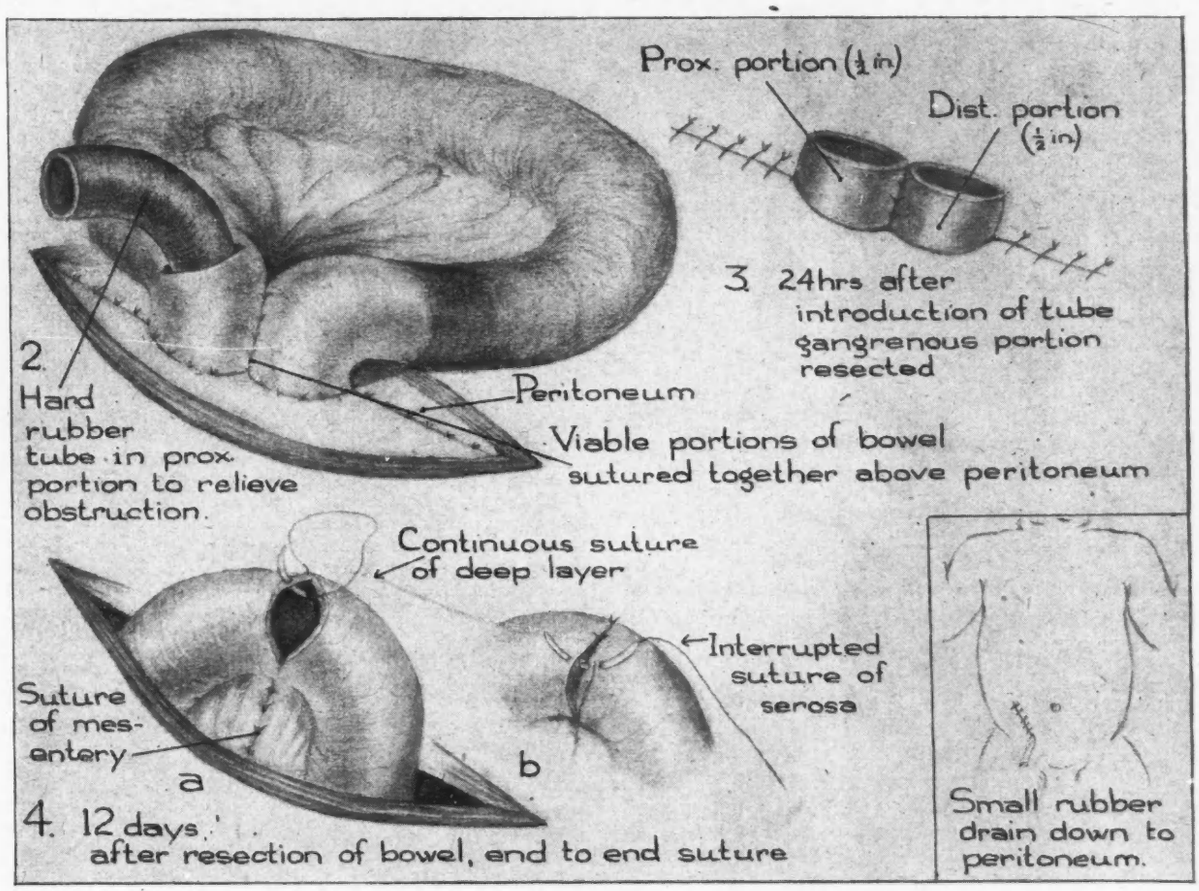
Prox. portion (½ in)
Dist. portion (½ in)
3. 24hrs after introduction of tube gangrenous portion resected
2. Hard rubber tube in prox. portion to relieve obstruction.
Peritoneum
Viable portions of bowel sutured together above peritoneum
Continuous suture of deep layer
Interrupted suture of serosa
Suture of mesentery
a
b
4. 12 days after resection of bowel, end to end suture
Small rubber drain down to peritoneum.

Fig. 2

In the manner just described, the following 4 cases were operated upon:

CASE 1 (1936)

H.M., aged 9 months. Previously in good health. Vomited 3 hours after feeding, blood passed by rectum, no bowel movement. Admitted 24 hours after onset of symptoms.

Physical examination.—Well developed, well nourished coloured baby in a poor state of hydration. Temperature 101.4°. Extremities hypertonic; mass in the right upper quadrant. Rectal examination revealed blood on the examining finger. Laparotomy performed and intussusception found with 6 inches of gangrenous terminal ileum. This was exteriorized. Twenty-four hours later the exteriorized gangrenous bowel was removed. Eleven days later the procedure was completed by an end-to-end anastomosis.

The child did exceptionally well and was discharged four weeks after.

CASE 2 (1940)

C.M., aged 9 months. Patient perfectly well until 4 days before admission, when vomiting occurred after each feeding and bright red blood was passed by rectum. This continued until admission.

Physical examination.—Infant poorly hydrated, with abdominal distension, and a half inch of bluish black bowel protruding from anus. Diagnosis: intussusception. Intravenous fluids were given immediately by means of a cut-down and a laparotomy was performed 3 hours after admission. The intussusception was reducible but the terminal ileum and ascending colon were gangrenous. Terminal ileum, cæcum and ascending colon were exteriorized. Forty-eight hours later, this 9-inch loop was removed. After 12 days, anastomosis was performed, and 2 days later patient was retaining fluids by mouth.

After a rather stormy postoperative course, the patient was discharged in good condition.

CASE 3 (1941)

C.T., aged 3 months. Patient was well a week before admission, when he became restless and cried and passed blood by rectum.

Physical examination.—Hydration fair. Abdominal distension and palpable mass in right lower quadrant. Rectal examination showed blood on examining finger. Diagnosis: intussusception. Laparotomy was performed

and an ileo-ileal intussusception secondary to a Meckel's diverticulum was found. This was treated according to the method previously outlined.

Patient made an uneventful recovery and was discharged 5 weeks after admission in good condition.

CASE 4 (1945)

J.G. This was a 6 weeks' premature baby, weight 5½ pounds. Vomiting 3 to 4 days, distended abdomen, swelling in right inguinal region with marked redness, tenderness and swelling of scrotum. Preoperative diagnosis: strangulated hernia. Child was in a marked state of dehydration. Intravenous fluids were started immediately.

Patient taken to the operating room. On opening into the hernial sac, 6 inches of gangrenous small bowel was found. The testicle was also gangrenous. The testicle was removed and the small bowel exteriorized. Twenty-four hours later the exteriorized bowel was resected. Four days following this operation, the proximal loop prolapsed. Child was taken to the operating room immediately and the prolapsed portion was resected and an end-to-end anastomosis performed. Patient continued to vomit for three days and it was decided to explore the site of the anastomosis. A band was found to be running from the site of the anastomosis obstructing the small bowel. At this time a side-to-side anastomosis was performed and the patient made an uneventful recovery. His weight on leaving hospital was 6½ pounds.

Since leaving hospital, the patient has done exceptionally well and now weighs 14 pounds.

SUMMARY

1. A three-stage operation for the surgical treatment of gangrenous bowel in infants under 1 year has been described.

2. Four successful consecutive cases, using the above procedure, are reported.

3. In addition to the operative procedures, the importance of adequate intravenous therapy, electrolytes and whole blood has been emphasized.

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"It must always seem strange that so long a time should have elapsed before the circulation of the blood and general physiology of the heart were understood. Even after Harvey's discovery but little knowledge of actual diseases of the heart was acquired for nearly a century. In fact one might say that knowledge of diseases of the heart hardly became a practical matter till auscultation and percussion came into general use in the early part of the nineteenth century.

CEREBRAL AIR EMBOLISM FOLLOWING ARTIFICIAL PNEUMOTHORAX; TREATMENT WITH PROLONGED INHALATION OF OXYGEN*

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THE following case history describes a clinical picture of cerebral air embolism which followed artificial pneumothorax. Untoward reactions occur occasionally after this therapeutic procedure. They vary in degree and severity; even the cerebral disturbances are variable. Some of the reactions result from pleural shock, *i.e.*, they have a reflex basis arising from the needling of the pleura, whereas others are clearly due to air embolism. In this instance air embolism was almost certainly responsible; the clinical opinion was backed by electroencephalographic evidence. Treatment by continuous inhalation of oxygen was used, with results worthy of comment and further application.

CASE HISTORY

The patient, a female of 28 years, suffered from bilateral apical tuberculosis, for which she had been receiving regular bilateral pneumothorax refills since the latter part of 1944. She had been sputum-free for 9 months prior to admission. For the previous 6 months the right pneumothorax was hard to maintain.

On March 21, 1946, the routine refill was carried out and 150 c.c. of air were introduced into the right side, final pressures being plus 4 to plus 8 centimetres of water. As the needle was being withdrawn the patient went into a violent convulsion. There was jerking of the face and jaw muscles, repeated clonic twitching of the extremities and opisthotonic arching of the back. Seizures recurred at short intervals for a period of 3 hours. During this time the patient was comatose, sweated profusely and was incontinent.

On the following day, she was transferred to the Royal Edward Laurentian Hospital (Laurentian Division) nearby. She was still in deep coma but was breathing regularly and freely. The left extremities were unresponsive and lifeless, but the right arm and leg thrashed restlessly in the bed, producing friction burns over pressure points. Musculature was spastic, deep tendon reflexes were increased and the Babinski sign was present bilaterally. The corneal reflexes were absent. The pupils were small and unresponsive to light. Lumbar puncture revealed normal fluid at a pressure of 110 mm. of water. During the patient's stay in the sanatorium the temperature followed a spiking course, reaching a high of 107 degrees. No real improvement in her clinical condition took place. Therapy consisted of sedation, intravenous feeding and penicillin.

On March 24 she was transferred to the Montreal Neurological Institute. She had then been comatose for approximately 3 days. Her left side was still lifeless,

* From the Neurological Service of the Montreal Neurological Institute and the Department of Medicine, Royal Victoria Hospital, Montreal. Dr. Herbert Jasper made the electroencephalographic studies. Dr. O. H. Warwick and Dr. A. M. Fraser were consulted concerning the prolonged breathing of oxygen in this case.

and the right underwent periodic purposeless movements. The pupils were moderately dilated, the right being slightly larger than the left, and the light reflexes were absent. All extremities remained spastic, the left slightly more than the right, and the reflexes remained hyperactive. Babinski's sign was still present bilaterally. Lumbar puncture produced clear fluid at normal pressure. Cells totalled 2 lymphocytes; Pandy was negative; Wassermann negative; and protein 80 mgm. % (upper normal 40 mgm. %). Other laboratory findings were: Urinalysis, negative; blood Wassermann, negative; Hgb. 82% (12.8 gm.); red blood cells 4.2 million; white blood cells 7,100; sedimentation rate 33, markedly increased.

On admission to the Institute the patient was fitted with a B.L.B. mask and supplied a mixture of carbon dioxide and oxygen. Within half an hour the mixture was replaced with 100% oxygen, which was given continuously, at 14 litres per minute, for the following 9½ hours. At the end of that time she was partially conscious and responded to questioning. Her articulation was clear and it was then learned that her left side was anæsthetic and a left homonymous hemianopsia was present. Over the next few days residual apathy, drowsiness and confusion gradually disappeared. All sedation was discontinued. Nicotinic acid was given to the point of flushing. By March 30, apart from a slight tendency to perseveration and a residual left hemiparesis, the patient was well.

After the acute stage of her illness was passed the status of her tuberculosis was investigated. It was decided to abandon the right pneumothorax, as it was very small and the disease in the right lung appeared to be minimal and quiescent. The left pneumothorax was to be continued with care and only so long as free space was available. The pressures, which were positive, were to be watched carefully.

Four electroencephalograms were obtained over a period of 6 months. The tracings revealed interesting evidence of marked generalized alteration of cortical function. Representative samples of the serial tracings are illustrated in Fig. 1. Summaries of the individual reports by Dr. Jasper are listed below:

March 25.—"The electroencephalogram indicates a severe generalized alteration in cortical function with complete depression of normal rhythms, and their replacement by low amplitude slow waves with some epileptiform discharge confused with muscle potential artefact. The generalized change in cortical activity could be explained either by a general change in metabolism of the entire cortex or, most probably in this case, by a lesion of the brain stem structures affecting rhythms from all cortical regions."

April 2.—"Some improvement is shown over the previous study, but there is persistence of very generalized slow wave abnormality indicating marked impairment of cerebral functions most severe in the right posterior hemisphere including the central region. There is some evidence of early development of cortical discharge."

April 8.—"This shows a slow, but definite improvement compared to the previous examination of April 2. There has been a decrease in abnormality, particularly from the left hemisphere, the right showing the more serious disorder at the present time."

October 9.—"There has been a very striking improvement in the electroencephalogram, consisting in diminution in slow waves, and increase in normal alpha rhythm. There is at present an area of depressed alpha activity over the right posterior occipital area principally, but extending also to the temporal region on the right. There were also some 4 to 6, and 7 per second slow waves observed over the central regions, chiefly from the right side. The very slow delta waves previously observed were completely absent. These results could suggest a residual impairment of normal function, particularly over the right centro-temporal and parieto-occipital regions, with possibly some involvement of radiations to the right parietal and occipital areas with very little evidence for any residual abnormality from the left hemisphere."

This patient has been examined on numerous occasions. She is still carrying the left artificial pneumothorax, receiving only 25 c.c. of air every 4 to 5 weeks. The pressures are always positive. The disease in the right lung remains apparently arrested. It has been decided that if her present condition continues the left artificial pneumothorax will be discontinued in the spring.

The neurological condition is apparently static. She has regained almost complete function and strength of the left leg, with good musculature and only slight spasticity. The left arm is of fair strength but is hard to use because of a flexion deformity at elbow and wrist with spasticity and wasting. The patient has returned to her former occupation and has gained weight.

Final neurological examination on January 24, 1947, showed increased deep reflexes on the left side of the body, with left ankle clonus. Babinski's sign could not be elicited. No part of the former hemianopia remained.

DISCUSSION

Accidents following artificial pneumothorax are continually being reported in the literature.[1 to 10] The frequency of such accidents varies to a remarkable degree in different clinics; compare the report of Jones and Lockhart[7] presenting an incidence of 1 in 6,073 treatments, with that of Warring and Thomas[11] reporting 1 reaction in 43 punctures. It is

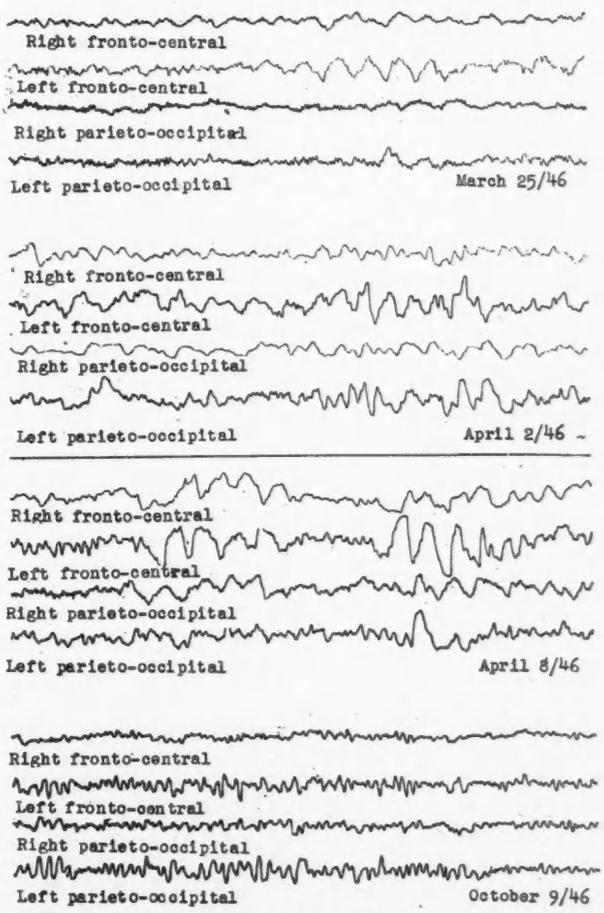

Fig. 1.—Serial electroencephalograms illustrating the almost total cessation of normal activity from the right side of the brain following the initial cerebral air embolism. Gradual recovery of normal cortical function can be seen with the decrease in slow waves and the increase in alpha waves from March to October, 1946.

possible that these differences are due to the absence of a uniform criterion as to what constitutes a "reaction".

The reactions, and fatalities, following artificial pneumothorax result from interference with one of the 3 major organs, the heart, the lungs, and the brain. Symptoms due to the plugging of the pulmonary arteries with emboli are the commonest of all, but the least likely to lead to serious sequelæ.[12, 13] Blocking of the coronary arteries is, on the other hand, the most serious accident. It is in regard to the cerebral manifestations that greatest controversy has arisen.

There seem to be two distinct types of reaction. (*a*) A reflex arrest of circulatory function arising from the needling of the pleura with resulting symptoms such as dizziness, syncope, cardiac arrest—a complex which is very similar to the vasovagal reflex effects of a hypersensitive carotid sinus. Capps, in his Billings Lecture,[14] has reviewed the evidence for such a reflex causation of symptoms, although other workers do not agree entirely with his views.[7] (*b*) The other type of reaction is different and is featured by convulsions, paralyses, blindness, anæsthesiæ and coma; in other words, a violent, shocking episode with diffuse interference in the function of the central nervous system such as multiple emboli might produce. This reaction is attributed to air embolism, first, because the cause and effect relationship is so striking, and, secondly, because the symptom complex resembles that which has been produced in animals by intravascular injection of air. Actual demonstration of air emboli occluding the vessels has proved a difficult technical procedure. Most embolic reactions are transitory; a few leave neurological sequelæ as in the case just reported, and an even smaller number are fatal. Dowd's important case[26] of death in a patient with pneumothorax at an altitude of 16,000 feet fits into this latter group. Convulsions and death occurred in twenty-eight hours.

In the case now reported, some portion of the 150 c.c. of air introduced into the chest gained entrance to the pulmonary venous system, passed through the left heart and into the cerebral circulation. There were no symptoms of pulmonary embarrassment. It will be recalled that after 150 c.c. of air were introduced into the apparently poor space in the right chest the final pressures were about plus 4 to plus 8 centimetres of water, a factor that might have a bearing on the flow of air into the pulmonary venous system. The early work of Brandes is quoted by Jones and Lockhart[7] to illustrate the mechanism of embolus production. He was irrigating an empyema cavity with bismuth paste when the patient suddenly went into spasm and developed deviation of the eyes. He died 20 hours later. At autopsy bismuth paste was found in the smallest blood vessels of the cerebral cortex of both hemispheres, and particles could be traced from the wall of the cavity into the pulmonary capillaries and veins.

OXYGEN BREATHING

The use of pure oxygen breathing in this case was suggested by the work of Behnke[15, 16] and Fine[17, 18, 19] who proved its value in displacing nitrogen from the blood and tissues. This use of oxygen has been amply confirmed by the experiences of Canadian and American investigators during the recent war. The authors were fortunate in having had some of this experience. Clinical application of this principle has been confined, in the main, to the treatment of aviators and caisson workers subjected to rapid atmospheric pressure change with consequent air embolus formation.

Pure oxygen breathing has also gained some use in the treatment of abdominal distension and post-pneumoencephalographic discomfort. Behnke has shown that 9 to 11 hours of pure oxygen inhalation will completely rid the body tissues of their nitrogen, although some variation can be expected because of different fat content in individuals.

Some difference of opinion exists regarding the length of time pure oxygen can be inhaled at atmospheric pressure without toxicity. In 1939 Behnke[20] stated that pure oxygen, administered at atmospheric pressures, would produce symptoms of bronchial irritation or vasomotor spasm in a matter of 6 to 7 hours. Subsequently, Boothby[22, 23] reviewed a series of 800 cases treated with pure oxygen for varying periods of time ranging up to 48 hours with no signs of pulmonary irritation. In a later publication Behnke[23] modified his view somewhat when he remarked that most healthy men tolerated oxygen for as long as 17 hours in his tests.

Before discussing how oxygen administration might be expected to improve the clinical status

of a patient such as this, we should have an idea of the probable pathological change in the brain. Air emboli, trapped in cerebral vessels, obstruct circulation and render portions of the brain anoxic. In addition to the mechanical obstruction they effect, they serve as irritating foci to provoke reflex spasm, with possible subsequent thrombosis and hæmorrhage, so that a combination of pathological changes may contribute to the final tissue destruction.[25]

Three mechanisms may be considered as having to do with the clinical improvement of this patient. First, it may have been coincidental and entirely unrelated to the administration of oxygen. It is a fact that patients who have suffered a cerebral accident will improve spontaneously in rather dramatic fashion. The other two possibilities relate to the administration of oxygen. Pure oxygen breathing raises oxygen concentration in physical solution in the plasma from a figure of 0.3 volumes % to between 2.0 and 2.2 volumes %, and in addition it aids in the outward diffusion of gaseous nitrogen from the lungs, leading to its eventual elimination from the blood and tissues. The inhalation of oxygen in pure form may aid in the nutrition of partially devitalized tissue, but the greater potentiality for benefit lies in its property of displacing nitrogen. In the case reported, breathing a 95% oxygen, 5% carbon dioxide mixture for half an hour produced no change whatever, so that a transient anoxia was not thought to be the underlying problem here, but rather air embolism.

CONCLUSIONS

Present day methods of treating air embolism following artificial pneumothorax are nonspecific and ineffectual. Fine, in 1940, referred to the helplessness of physicians in such circumstances and deplored their failure to follow up the implications arising from Behnke's work. This report will have served a purpose if it stimulates further use of pure oxygen breathing over long periods to combat the unfavourable effects of cerebral air embolism immediately following the introduction of air into the circulation.

SUMMARY

1. A case of cerebral air embolism following artificial pneumothorax is presented. Initial convulsions, coma, hæmianopsia and hemianæsthesia disappeared, but there was a residual left-sided hemiparesis.

2. Serial electroencephalograms show the obliteration of normal cortical activity in this instance, with a gradual return towards normal.

3. The continuous breathing of pure oxygen for a period of 9½ hours, even though delayed for an interval of 3 days, was associated with marked improvement.

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RÉSUMÉ

Présentation d'un cas d'embolie cérébrale gazeuse consécutive à un pneumothorax artificiel. Le syndrôme neurologique présenté: (convulsions, coma, hémianopsie et hémianesthésie) disparut mais il persista un certain degré d'hémiparésie gauche. Des E.E.G. en série démontrèrent l'arrêt de l'activité corticale normale, de même que le retour graduel à la normale. La malade présentée respira de l'oxygène pur pendant 9½ heures. Les mécanismes d'action de l'oxygène sont discutés; aucun n'est définitif. L'hypothèse la plus séduisante serait la sortie des poumons du nitrogène gazeux et son élimination du sang et des tissus tandis que l'oxygène redonnerait de la vitalité aux tissus.

JEAN SAUCIER

THE MANAGEMENT OF ASTHMA*

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THE asthmatic patient is one who is prone to attacks of difficult breathing. The diagnosis of asthma, however, is, in some cases, not as simple as some suppose. As Rackemann has aptly said "all is not asthma that wheezes", and indeed not infrequently asthma erroneously has been diagnosed in the absence of any "wheeze". For example, many cardiologists employ the term "cardiac asthma" to designate those attacks of spasmodic non-wheezy dyspnœa occurring at night in patients with left ventricular myocardial failure. This is very confusing since the mechanism is entirely different from that of true asthma. A better name would be paroxysmal nocturnal dyspnœa, but of course that designation has the disadvantage of being clumsy.

The immediate mechanism producing asthma has been known since 1698 when Floyer described spasm of bronchial musculature plus turgescence of the bronchial mucosa as the cause of the difficult breathing. These features are frequently accompanied by bronchial occlusion from mucous gland secretion. The fundamental and more remote mechanism has been studied intensively, especially during the past twenty-five years, but much still remains to be elucidated. It is not within the compass of this paper to review in detail what is now known but certain basic factors must be understood before a rational approach to the problem of management and specific treatment is possible.

FUNDAMENTAL CAUSES OF ASTHMA

The phenomena of the asthmatic attack are believed to be due to an allergic response on the part of the susceptible individual to certain stimuli affecting the shock organs of the body (in this case the bronchial tree). This belief in the rôle of allergy in creating the background for asthma is probably justified if we accept a liberal interpretation of the term allergy. According to this concept, we must differentiate between atopy, or atopic allergy, and bacterial allergy as exemplified in the patient who develops asthma as the direct result of infection in some part or parts of the respiratory tract. Such a differentiation must precede any attempt to lay down a plan for the management of any individual case.

TABLE I.

Atopy	*Bacterial allergy*
Demonstrated by scratch or intracutaneous skin tests. Positive in hay fever and atopic asthma.	Demonstrated by scratch (von Pirquet) or intracutaneous (Mantoux) skin tests. Useful in tuberculosis. Not applicable in asthma.
Skin reaction is "immediate" (15 to 30) minutes.	Skin reaction is "delayed" (48 hours).
Skin reaction is urticarial in nature.	Skin reaction is inflammatory in nature.
Disease is hereditary.	Hereditary nature not definitely established.

The two most useful procedures leading to this differentiation are (*a*) a careful history and (*b*) protein skin tests, properly performed and carefully appraised. Elimination diets, such as suggested by Rowe may be necessary in cases where food allergy is suspected, as it is generally agreed that skin tests for foods are not infrequently falsely negative.

Granted, then, that an allergic state is the basic cause of asthma, it is necessary for the successful management of the asthmatic patient, to realize that certain diverse factors often quite unrelated to allergy may be the immediate or precipitating causes of individual attacks. Rackemann has illustrated this point by likening the allergic patient to a loaded gun. So long as the trigger is not pulled the gun will not go off. So long as the allergic patient avoids the precipitating factors, attacks of asthma will not occur. As just indicated, these factors are very diverse. First, of course, must be mentioned the specific substances to which the patient may be atopically allergic. Next we may call attention to infections of the respiratory tract, such as the common cold, attacks of acute tracheo-bronchitis, sinusitis and pharyngitis. But there are many factors which seem to irritate the bronchial tree in a non-specific way and thus set up an attack. Prominent among these are exposure to frosty air, strong fumes, perfumes and odours, dusty atmospheres in industrial plants, in the vicinity of coal furnaces being shaken down for the removal of ashes, or during the erasure of blackboards in schools, exposure to emotional upsets, violent exertion, night air (dampness),

* Read before the Royal College of Physician, Ottawa, November 16, 1946.

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a full stomach as after a hearty evening dinner, a horizontal position as in sleep, etc. These are the "trigger-pullers", and they must be recognized and understood by the physician and patient alike in the successful management of the case.

TABLE II.
IMMEDIATE PRECIPITATING FACTORS IN ASTHMA ("TRIGGER-PULLERS")

1. Excitement; emotional upsets.
2. Exposure to frosty air; "night air".
3. Exposure to dust, fumes, strong odours.
4. Exertion; coughing, hearty laughing.
5. Fatigue, "depletion".
6. Horizontal position, as in bed.
7. Respiratory infections; "catching cold".
8. Hearty meals (a full stomach).

PRINCIPLES OF TREATMENT

The first principle of treatment in any disease is to remove the cause. In the individual subject to asthmatic attacks, this would mean the abolition of the allergic state. The specific treatment of an atopically allergic patient constitutes a rational attempt to reach this goal. This may be illustrated by the series of preseasonal inoculations with extracts of pollens in the case of pollen asthma, or a similar series of inoculations with extracts of horse dander in the case of horse-sensitive patients.

TABLE III.
POLLEN DESENSITIZATION

Preseasonal weekly schedule

1/12,500 dilution—0.2 c.c.	1/2,500 dilution—0.2 c.c.
0.3 c.c.	0.3 c.c.
0.45 c.c.	0.45 c.c.
0.6 c.c.	0.6 c.c.
1/500 dilution—0.15 c.c.	1/100 dilution—0.1 c.c.
0.2 c.c.	0.15 c.c.
0.3 c.c.	0.2 c.c.
0.45 c.c.	0.3 c.c.
0.6 c.c.	0.4 c.c.

The results of such treatment are, in general, highly satisfactory. This procedure represents an attempt to "unload the gun".

In the case of individuals whose allergy is of the bacterial type we are confronted with a much more difficult task. Removing the cause would mean removing the infection. Inoculations with vaccines made from the offending bacteria would seem to offer the best hope of success, at least in theory. In practice, however, the results are not brilliant and, indeed, are often disappointing. Nevertheless, I am of the opinion that such an attempt should be made as it seems to me that in certain cases definite benefit can be achieved. In cases where the infection seems to originate in the upper respiratory tract, such as in the antra or other accessory nasal sinuses, it would seem logical to carry out whatever local treatment seems indicated to render these areas as free of infection as possible, but radical operations on the sinuses have proved disappointing in general and great care in the selection of cases for operation must be exercised. Simple operations such as the removal of polypi often result in considerable relief since these measures improve the airway and probably lessen the likelihood of reflex spasm of the bronchi.

So much for the removal of the cause of asthma. It is readily seen that this ideal goal is difficult, and in many cases impossible to achieve. What, then, can be done for those in whom the removal of the allergic state is beyond our power? This brings us to the second principle of treatment, namely avoidance of the allergen. Where this is a comparatively simple matter, as for example by getting rid of a domestic animal such as a cat or dog, the results are highly satisfactory. Avoidance of house dust is, on the other hand, a difficult problem for the average housewife, because in these days almost all of them are doing their own work. Installation of air conditioning in the house as a whole or even in a single bedroom is desirable but expensive. The wearing of a simple surgeon's gauze mask, preferably moistened, will often help, especially when engaged in dusty jobs. Where feathers must be eliminated it is necessary to exclude eiderdowns and cushions as well. The covering of pillows with "allergen-proof" material is not satisfactory because the seams, or zipper, closing the cover must allow fairly free egress of air or the pillow takes on the nature of a football. Such egress of air carries with it the very dust which the patient should avoid. Sponge rubber pillows, while not so soft are dust- and feather-free. There is no good in taking the feathers away from one spouse and allowing the other to sleep on feather pillows in the same room.

The avoidance of foods presents special problems. Where the offending food is of minor importance or non-essential, as in the case of celery, lobster or strawberry, avoidance is a comparatively simple matter. All that is required is a knowledge of the composition of

culinary preparations so that the foods concerned do not present themselves in disguised or unrecognizable form. For example, I have a patient who is very sensitive to onion. He was sure he was getting no onion in his food but his asthma continued to trouble him. I was sure he was not getting onion at home but not so sure about his lunches at his club. I called the chef at his club who informed me that the bouillon which my patient almost invariably had at lunch was flavoured with onion. Relief from the asthma was prompt when he omitted bouillon from his lunch.

In the case of essential foods or foods of major importance in the diet, avoidance is often undesirable, and desensitization shoud be resorted to. This is particularly the case in growing children who are allergic to milk, eggs or wheat. Inoculation by hypodermic injection of suitable extracts of the food or oral desensitization by gradually ascending doses of the food by mouth, usually prove effective.

TABLE IV.

ORAL DESENSITIZATION*

EGG

Directions: Beat an egg so that yolk and white are well mixed; then add the prescribed amount of egg to ordinary water and mix well. Take one teaspoonful of solution once a day, unless otherwise directed. Throw away the rest of the solution. Make up a fresh solution every day. Use a dilution of the same strength every day for four days.

Amount of egg in teaspoonfuls	*Amount of water*	*Special directions*
¼.....	2 quarts	take ¼ teaspoonful
¼.....	3 pints	" ¼ "
¼.....	2 quarts	" ½ "
¼.....	3 pints	" ½ "
¼.....	2 quarts	" 1 "
¼.....	3 pints	" 1 "
½.....	2 quarts	" 1 "
½.....	3 pints	" 1 "
1.....	2 quarts	" 1 "
1.....	3 pints	" 1 "
1.....	1 quart	" 1 "
2.....	3 pints	" 1 "
1.....	1 pint	" 1 "
2.....	1½ pints	" 1 "
1.....	1 cup	" 1 "
2.....	1½ cups	" 1 "
1.....	½ cup	" 1 "
2.....	¾ cup	" 1 "
1.....	¼ cup	" 1 "
1.....	3 tablespoonfuls	" 1 "
1.....	2 "	" 1 "
2.....	3 "	" 1 "
1.....	1 "	" 1 "
4.....	3 "	" 1 "
2.....	1 "	" 1 "
	Take 1 teaspoonful of raw egg.	
	Take 1½ teaspoonfuls of raw egg.	
	Take 2 teaspoonfuls of cooked egg.	
	Take 3 teaspoonfuls of cooked egg.	
	Take 4 teaspoonfuls of cooked egg.	
	Take ½ cooked egg.	
	Take ¾ cooked egg.	
	Take a whole egg.	
	After this eat at least 1 egg every few days.	

* From Keston, Waters and Hopkins: *J. Allerg.*, **6**: 531, 1935.

TABLE V.

MILK*

Directions: Take 1 teaspoonful every day unless otherwise directed. Make up a fresh solution every day.

Amount of milk	*Amount of water*	*Special directions*
1 teaspoonful	1 quart	
1 tablespoonful	2 quarts	
1 teaspoonful	1 pint	
1 tablespoonful	1 quart	
1 teaspoonful	1 cup	
1 tablespoonful	1 pint	
1 teaspoonful	½ cup	Use a dilution of the same strength every day for four days.
1 tablespoonful	1 cup	
1 teaspoonful	¼ cup	
1 tablespoonful	½ cup	
1 teaspoonful	2 tablespoonfuls	
1 tablespoonful	¼ cup	
1 teaspoonful	1 tablespoonful	
1 tablespoonful	2 tablespoonfuls	
2 teaspoonfuls	1 tablespoonful	
Take 1 teaspoonful of milk		
Take 1½ teaspoonfuls of milk		
Take 2 teaspoonfuls of milk		
Take 3 teaspoonfuls of milk		
Take 4 teaspoonfuls of milk		
Take 2 tablespoonfuls of milk		
Take 3 tablespoonfuls of milk		
Take ¼ cup of milk		
Take ⅓ cup of milk		
Take ½ cup of milk		
Take ⅔ cup of milk		
Take 1 cup of milk		

* From L. Tuft: Clinical Allergy, Saunders, Phila., 1937.

The third principle of treatment is the careful avoidance of what we have termed the "trigger-pullers". The physician and his patient must make a meticulous survey of nonspecific factors which precipitate attacks and list every circumstance which seems to have a bearing in this connection. This list should then constantly be borne in mind by the patient and every effort made to live in such a manner that these factors are eliminated so far as possible.

We now come to a consideration of the fourth principle in the management of asthma, namely immediate palliation of the symptoms while these other measures are under way towards what we hope will be the permanent control of the asthmatic attack. Temporary control may be obtained by a combination of the use of various drugs, of which epinephrin is still the most effective. However, its influence lasts only two hours, which is a serious defect. The smallest amount which will relieve the dyspnœa is the dose of choice. Hence we find that 3 to 5 minims of the 1-1,000 dilution given

hypodermically will often produce the effect and side reactions are avoided. Sprays of concentrated epinephrin orally administered during inspiration are often a godsend in milder attacks. Aminophyllin gr. 7½ given intravenously very slowly will often ensure freedom from attacks for eight to ten hours. Given by rectum in suppository form, it is ineffective, but in aqueous solution in doses of 9 or 10 grains in 20 c.c. of water is frequently almost as effective as in the intravenous route, and has the great advantage of enabling the patient to undertake self-administration. Ephedrin either alone or better in combination with a barbiturate given orally in capsule form will often be extremely useful. Various capsules containing aminophyllin, theamin, ephedrin, etc. together with a barbiturate are readily available. Potassium iodide in doses of 10 grains three times a day is a time-honoured remedy and still has a place in the treatment of the chronic asthmatic.

The severe cases should be admitted to hospital where tents or B.L.B. masks are readily available for oxygen administration and where intravenous and hypodermic therapy can be given at any time of day. Visitors should be excluded and the environment should be as quiet and placid as possible. The diet, excepting in those patients who are allergic to certain foods, should be general, simple and served frequently and in small amounts, as a full stomach frequently initiates asthmatic attacks. If, due to the severity of the illness, the intake is seriously restricted, vitamin supplements are indicated. The inhalation of fumes from burning asthma powders should be discouraged, since the relief obtained is purchased at the cost of further irritation of the bronchial mucosa. Tobacco should be proscribed for the same reason.

Few allergists believe that morphine has a place in the treatment of the asthmatic attack. Apart from the possibility of addiction in a chronic disease there is a real danger of depressing the respiratory centre at the very time that the patient is fighting for his breath with every ounce of energy he possesses, and the slowing of respiration from morphine may be the determining factor in causing death from asphyxia.

There is no question that many asthmatics find relief from their symptoms on moving to a more suitable climate. For most patients, the domestic and/or the economic problems involved make this expedient impossible. Where it is feasible, the physician must determine the factors which govern the choice of locality or climate for each individual case. For example, if it is a matter of pollen sensitization, the choice will be determined by the vegetation to be encountered. Where respiratory infection, and the deleterious effects of cold and dampness are major factors, a southern area in the dry belt where mildness and dryness characterize the winter climate will usually be found to be most suitable. In any event, and particularly in cases where a move involves considerable sacrifice from the domestic and economic standpoint it should be made clear to the patient that such a project must be approached with the clear understanding that no guarantee can be given as to the results. One can only say that in selected cases much improvement is frequently experienced and therefore the experiment (for such it is) is justified.

SUMMARY

General principles governing the management of asthma are laid down. These are based on etiology. The fundamental etiological factor is an allergic state of the individual. The allergy may be atopic, bacterial or both. The principles of treatment are: (1) Removal of the cause (desensitization). (2) Avoidance of the allergen. (3) Avoidance of non-specific "trigger-pullers". (4) Immediate treatment of the attacks.

SPINAL CORD CIRCULATION IN POLIOMYELITIS. — A study of the distribution of paralysis in 1,200 poliomyelitis patients at the Harvard Infantile Paralysis Clinic (1925-41) showed that there is a significant preponderance of paralysis of the left arm over paralysis of the right. When the limb is involved at all, more than two-thirds of its muscles on the average show demonstrable paralysis 3 weeks to 3 months after use, although over 95% of all poliomyelitis cases have at least one limb which escapes paralysis. The author suggests that alteration of the circulation of the spinal cord may be a factor in determining this selective distribution, and instances 5 cases in which residual paralysis was localized to a limb, or limbs, which had previously been subjected to strain or trauma. Reference is made to experimental attempts (at present in progress) by paravertebral block to alter the circulation of the spinal cord in animals and human beings with poliomyelitis, with a view to changing the course of the disease.—N. Nelson, *Science*, **104**: 49, 1946.

FOLIC ACID IN THE TREATMENT OF PERNICIOUS ANÆMIA*

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THE name "folic acid" has been applied to a group of closely related substances which promote the growth of certain bacteria used as test organisms (*Lactobacillus Casei* and *Strep. fæcalis*) and which have anti-anæmic properties. It was applied first to a highly purified extract from spinach (hence the name) obtained by Mitchell, Snell and Williams[1] in 1941. Similar substances had been isolated previously from yeast by Stokstad and Manning[2] among others and from liver by Pfiffer *et al.*,[3] the latter being called vitamin B$_c$. The product synthesized by Angier and his fifteen co-workers[4] in 1945, has been referred to as folic acid though called by them the "L. Casei" factor.

This synthetic folic acid has received a considerable clinical trial. It has been reported as beneficial in various types of macrocytic hyperchromic anæmias by Spies *et al.*,[5] Darby *et al.*,[6] Moore *et al.*,[7] Kaufmann and Schwager,[8] Zuelzer,[9] Doan *et al.*,[10] and Amill and Wright.[11]

We have had the opportunity to use synthetic folic acid on the four following cases of pernicious anæmia to date.

CASE 1

Mrs. M.M., aged 46 years, admitted May 21, 1946, complaining of weakness, especially during the past month and numbness of the legs with pain in the feet.

Physical examination revealed a grey haired lady looking older than her forty-six years, with notable pallor of the skin, a smooth tongue, a palpable spleen and loss of vibration sense below the knees. All blood counts before and during therapy are shown on Fig. 1. It will be noted that prior to treatment the average erythrocyte count was 1,290,000 per c.mm.; the hæmoglobin estimation averaged 5.9 gm. per 100 c.c. The colour index was 1.5. The average white cell count was 3,825 per c.mm. with 53% polymorphonuclear neutrophils. The reticulocytes numbered 2% of the red cells. The mean cell diameter was 8.6 microns.

Macrocytosis, marked poikilocytosis, anisocytosis and megaloblasts were seen in the stained blood smears. The sternal marrow biopsy showed a typical megaloblastic reaction.

The gastric analysis, after administration of histamine 0.3 mgm., was negative for hydrochloric acid. The van den Bergh was 1.2 mgm. %. Chest x-ray and barium examination of stomach and duodenum were normal. No occult blood was detected in stools.

With a diagnosis of pernicious anæmia treatment was begun with folic acid, 10 mgm. daily I.M. with results as noted in Fig. 1. By the 5th day the patient noted subjective improvement. The reticulocyte peak was 23% on the 6th day of treatment.

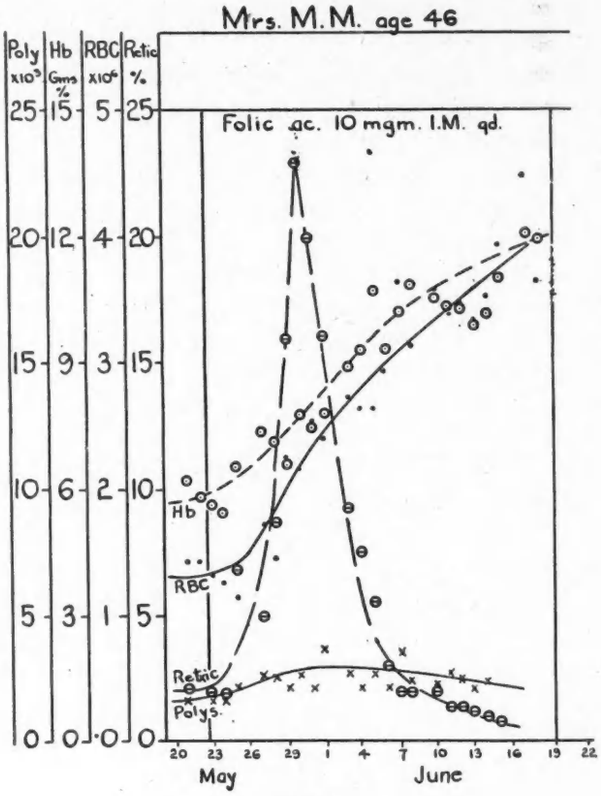

Fig. 1

The red cell count increased by 800,000 during the first week, another 700,000 during the second week, 600,000 the third week and approximately 500,000 during the fourth week of folic acid treatment.

The polymorphonuclear count improved toward the end of the first week of treatment. Although the reticulocyte peak was less than the standard for liver,[12] the erythrocyte increase was better than expected under adequate liver therapy,[13] as was our estimate of the subjective improvement.

CASE 2

Mrs. I.K., aged 57 years, admitted July 12, 1946. This patient gave a history of increasing weakness with a gradual onset and slow development until two to three months previous to admission when it became marked so that household duties could no longer be performed.

Physical examination was negative except for a smooth tongue and a slightly icteric skin with marked pallor. Neurological investigation was negative.

Admission blood count was red blood count 1,270,000, hæmoglobin 6.4 gm. %, colour index 1.7, white blood cells 2,100 with 62% P.M.N. of which 12% were stab forms; macrocytosis and poikilocytosis were noted as well as a few megaloblasts; the reticuloeyte count was 6%. Other pertinent laboratory information included a gastric analysis free of hydrochloric acid after stimulation with 0.6 mgm. of histamine, and a van den Bergh of 2.16 mgm. per 100 c.c.

Folic acid 10 mgm. per day intramuscularly was begun on July 15, 1946. During the first week reticulocyte counts were somewhat variable but increased on the average. The erythrocyte increase was approximately 300,000 cells per c.mm. The polymorphonuclear count remained at a low level. By the fourth day of treatment the patient reported that she felt much better. As laboratory evidence of improvement was somewhat slow (Fig. 2) the folic acid dosage was increased to 20 mgm. I.M. daily beginning on the ninth day of treatment but in spite of this the second week's progress seemed none too promising. The reticulocyte peak of nearly 10% was reached on the twelfth day of treat-

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ment, the erythrocyte increase during this week was between 200,000 and 300,000. The hæmoglobin gave more encouraging evidence of improvement as did the hæmatocrit, which was 18% on the second day of treatment and 32% two weeks later. Subjectively the patient was considerably stronger.

The third week saw very satisfactory improvement. The erythrocyte count increased by nearly a million cells per c.mm., the hæmoglobin increased similarly and the polymorphonuclear count rose somewhat. The reticulocyte count fell rapidly and after three weeks of folic acid therapy, the patient was put on liver to be continued after discharge from the hospital.

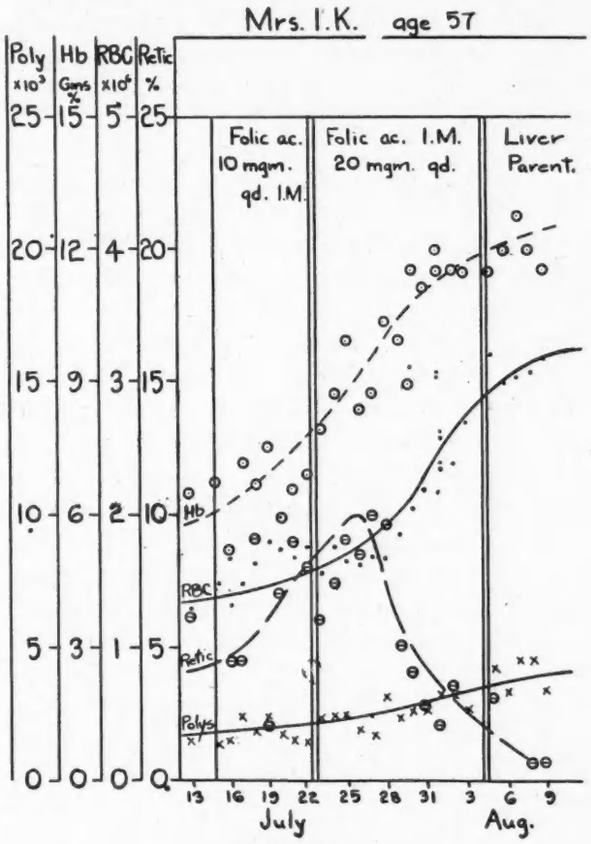

Fig. 2

In spite of the fact that there was evidence suggestive of a natural remission at the beginning of treatment (the reticulocyte count being elevated) yet the improvement in the erythrocyte count in this case was below the standards of Isaacs[13] during the first and second week by about 50%. This was almost completely made up during the third week, possibly due to the fact that the dosage had been increased to 20 mgm. daily. The reticulocyte response was definitely lower than that expected under liver therapy.[12]

CASE 3

Mrs. S.McK., aged 58 years, admitted July 27, 1946, with a history of pernicious anæmia for three years with sporadic and inadequate treatment and a severe relapse beginning four to five weeks prior to admission, leading to effort pain substernally as well as marked weakness and a sensation of numbness in the legs and arms.

Examination showed marked pallor, grey hair, smooth tongue, loss of vibration sense below the knees and a systolic murmur at the apex and base of the heart. Blood pressure was 102/60. The blood van den Bergh was 1.1 mgm. per 100 c.c. The urine was normal and there was no occult blood in successive stools. The x-ray of chest showed a cardiothoracic ratio of 0.61. The electrocardiograph showed no definite abnormality. Gastric analysis showed no free HCl after histamine 0.5 mgm.

The blood counts prior to and after treatment are charted (Fig. 3). Before treatment the average of three counts was: erythrocytes 1,730,000; hæmoglobin 6.4 gm. per 100 c.c.; leucocytes 2,750 of which polymorphonuclears were 39%; reticulocytes 0.8%. Successive halometer readings gave a mean cell diameter of 8.4 microns. Packed cell volume was 22%. The calculated mean corpuscular volume on this data was 127 cu. microns, the mean corpuscular hæmoglobin was 37 micrograms and the mean corpuscular hæmoglobin was 37 micrograms and the mean corpuscular hæmoglobin concentration was 29%.

The diagnosis of pernicious anæmia was considered definite and the case was treated with folic acid, 20 mgm. I.M. daily starting on July 31, 1946. Progress was satisfactory (See Fig. 3).

The reticulocyte response was evident in six days, reaching a peak of approximately 6% on the tenth day. The red cell response showed an increase of 600,000 in the first week, and a similar increase on the average during the second, third and fourth weeks of treatment at the end of which time the erythrocytes numbered 4.2 million per c.mm. This was better than the standards of Isaacs[13] obtained with liver therapy.

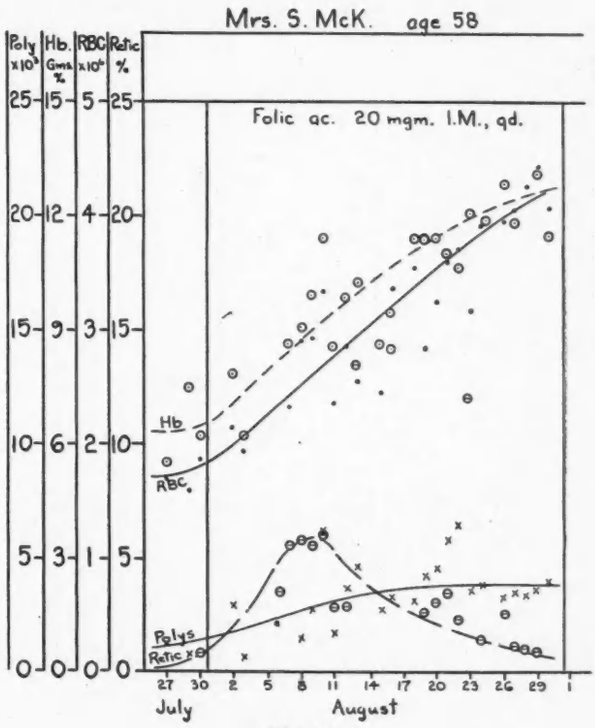

Fig. 3

Definite subjective improvement was claimed on the third and fourth days of treatment, so far as a sense of well-being and the appetite were concerned. By the end of the first week of treatment vibration sense had returned sufficiently to appreciate the tuning fork at the ankles.

During the course of treatment the patient developed a paroxysm of auricular fibrillation lasting about thirty-six hours.

CASE 4

Mr. P.H., aged 67 years, admitted July 22, 1946. This patient gave a history of chronic bronchitis with frequent acute flare-ups since childhood, weakness and loss of appetite of three weeks' duration.

Clinical examination revealed evidence of chronic infection with râles, an emphysematous chest and clubbing of the fingers. The neurological examination was negative. Laboratory investigations revealed evidence of anæmia with an abnormally high colour index. For initial blood counts and subsequent progress see Fig. 4.

Averaging the first five counts the erythrocytes numbered 2,350,000 per c.mm.; the hæmoglobin was 10 gm. per 100 c.c.; the leucocytes averaged 6,000 with 60% polymorphonuclear neutrophils.

On July 30, the cell diameter was repeatedly measured by the halometer method, readings of 8.3, 8.5, 8.6, and 8.5 microns being obtained by a technique which with the same observer and several samples of normal bloods resulted in readings between 7.0 and 7.6. The packed cell volume was 31% at 3,000 r.p.m. until constant. Taking the average of the cell counts done on July 30 together with the packed cell volume, the mean cell volume was 129 cu. micron (normals being 82 to 92). The mean corpuscular hæmoglobin was 42 micrograms (normal being from 27 to 31) and the mean corpuscular hæmoglobin-concentration was normal at 32.5%. The reticulocyte count was 1.1%.

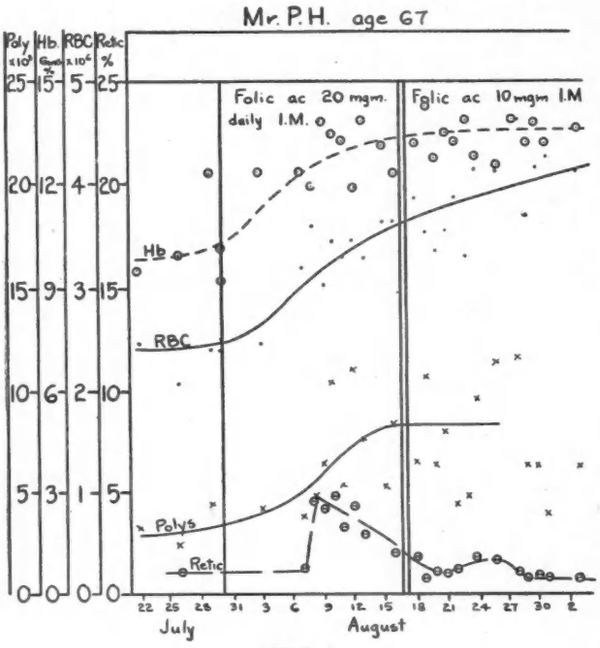

Fig. 4

The gastric analysis was negative for free hydrochloric acid after 0.5 mgm. of histamine. There was no evidence of blood loss in stools or urine.

With the above positive laboratory findings, this case was considered one of pernicious anæmia and treatment by 20 mgm. of folic acid I.M. daily was instituted on July 30.

The subsequent progress was satisfactory. The reticulocyte response began on the ninth day reaching only 4.9%, on the eleventh day, thereafter gradually subsiding to values approximating 1% after the nineteenth day. The gain in the red cell count was 600,000 in the first week, a further 500,000 in the second week and 200,000 to 300,000 in each of the third and fourth weeks, which is quite comparable to the standards of Isaacs[13] for adequate liver therapy.

Subjectively the patient reported improvement in his appetite and his general feeling of well being by the fifth day of therapy. After 18 days the folic acid was reduced to 10 mgm. daily.

The above four cases were consecutive admissions suffering from pernicious anæmia. The results of folic acid therapy were highly satisfactory both subjectively and according to the laboratory results.

In order to obtain a more valid picture of the effectiveness of the folic acid therapy in pernicious anæmia, we have analyzed 18 cases collected from the literature[5, 7, 8, 10, 11] along with our own. The results appear in Table I. Progress has been judged according to the reticulocyte response and the red blood cell increase. In each case the standards of Isaacs[13, 14] have been used for comparison. The grading "plus" was given if this response was more than 20% over standard. "Average" included cases within plus or minus 20% of the respective standards. Cases below "average" but above 50% of standard were graded "fair" and if below

TABLE I.

Source	*Case No.*	*Folic acid dosage*	*Reticulocyte response*	*Erythrocyte response*	*Comments*
Spies[5]	7	20 mgm. I.V.	Poor	Fair	
	8	20 mgm. I.V.	Fair	Average	
	9	20 mgm. I.V.	Poor	Poor	Initial red blood cell count doubtful
	10	100 mgm. orally	Fair	Fair	
	11	100 mgm. orally	Plus	Average	
Moore, *et al.*[7]	1	100 mgm. orally	Plus	Average	
	2	30 mgm. orally	Plus	Average	
Doan, *et al.*[10]		2 mgm. I.V.	Average	Fair	Increase to 10 mgm. on 20th day
Kaufmann and Schwager[8]	1	20 mgm. orally	Poor	Plus	
	2	30 mgm. orally	Plus	Average	
	3	40 mgm. orally	Average	Average	
	4	30 mgm. orally	Plus	Average	
Amill and Wright[11]	1	100 mgm. orally	Poor	Plus	
	2	100 mgm. orally	Fair	Average	150 mgm. 1st day then skipped 2 days
	3	100 mgm. orally	Fair	Average	
	4	20 mgm. I.M.	Fair	Average	1st 3 doses 75, 50 and 25 mgm.
	5	20 mgm. I.M.	Fair	Fair	1st day 75 mgm.
	6	25 mgm. I.M.	Average	Plus	Initial dose 75 mgm., total 1st week 550 mgm.
Authors' cases	1	10 mgm. I.M.	Fair	Plus	
	2	20 mgm. I.M.	Poor	Average	10 mgm. per day for 1st week
	3	20 mgm. I.M.	Poor	Average	
	4	20 mgm. I.M.	Average	Average	

this the case was classed as "poor". The erythrocyte responses were graded according to the weekly progress of the case whenever the data would permit. Hæmoglobin estimations were given some weight. The grading was thus intended to give an over-all picture of the red cell response. With the reticulocyte peak the grading was of course simpler.

It will be noted from Table I that the reticulocyte responses tended to be rather sub-standard. In 9 of 22 cases it was "average" or better, in 7 it was "fair" and in 6 "poor".

The erythrocyte response to folic acid therapy was generally more satisfactory than the reticulocyte response. It will be seen from the tabulated data that there was only one case in which the red cell increase was "poor". In it the initial count was considered erroneously high. There were 4 cases classed as "fair". The rest were "average" (13 cases) or even better (4 cases).

In the first 8 cases in Table I, a diet free from "extrinsic factor" was prescribed. These cases include 4 of the 5 sub-standard erythrocyte responses. One of these was doubtful and another received the least amount of folic acid.

It is to be noted in Table I that the reticulocyte response in these cases was not particularly in accordance with the red cell increase. In the 6 cases in which the reticulocyte response was "poor" the cell increase was graded "plus" twice, "average" twice, "fair" once and "poor" once. One should not then be discouraged in the use of folic acid in pernicious anæmia on finding a poor reticulocyte response. Incidentally, in all but one of the cases studied the reticulocyte peak came between the fifth and the twelfth days of treatment inclusive. In the exceptional case the dosage for the initial period was only 2 mgm.

One may conclude from Table I that folic acid in doses of 20 to 30 mgm. daily by mouth or 10 to 20 mgm. intramuscularly is satisfactory in the treatment of pernicious anæmia in relapse. Concerning the effective maintenance dose of folic acid, we have insufficient information to justify any conclusions.

The early improvement such as we observed in our cases, especially the alleviation of some of the subjective neurological symptoms, would suggest that folic acid might be the equal of liver in its ability to delay or prevent the development of subacute combined degeneration of the spinal cord. This must remain only a hope until years rather than weeks of experience have accumulated.

It is interesting to speculate on the possible relationship of folic acid to the extrinsic and intrinsic factors of Castle[14] and to the product of their interaction, absorption and storage in the liver. Obviously folic acid is not identical with the extrinsic factor or it would not be therapeutically effective orally in the absence of the intrinsic factor, that is, in the pernicious anæmia patient. Nor can it be closely related to the intrinsic factor, as it is effective in cases[5, 7, 10] in which the extrinsic factor was eliminated. It has been postulated by Sturgis[15] that the folic acid might be a principle held in the food in a bound or fixed form from which it is ordinarily liberated by a ferment present in normal gastric juice. In its free form it would not require the action of normal gastric juice and would be effective in pernicious anæmia therapy.

One would expect in any case that folic acid would be closely related to the fundamental anti-pernicious-anæmia factor such as is present in potent liver extracts. However, there are very marked differences between the two. The latter has a molecular weight estimated at between 5,000 and 10,000, and appears to be a polypeptide in structure.[16] Folic acid, at least the natural variety, is thought to have a molecular weight around 400 and it can be crystallized,[17] whereas the larger molecule of the liver factor has only been obtained in a somewhat impure amorphous form. Yet extracts of this latter factor have been obtained in sufficiently concentrated form so that they are effective therapeutically in a dose of 1 mgm.[18] Again commercial liver anti-pernicious-anæmia extracts contain only 0.25 to 0.5 micrograms of folic acid per c.c.[19] Thus the therapeutic efficiency of these liver fractions in pernicious anæmia is out of all proportion to their folic acid content. The evidence as interpreted to date seems to indicate that folic acid is a substance effective in pernicious anæmia therapy but otherwise unrelated to the intrinsic or extrinsic factors of Castle[14] or to the anti-pernicious-anæmia factor in liver.

SUMMARY AND CONCLUSIONS

Folic acid, a synthetic substance similar to a member of the vitamin B complex, has been used in the treatment of pernicious anæmia.

Four cases are reported in which it was the sole therapeutic agent.

Twenty-two cases, 18 collected from the literature, have been analyzed. From these it would appear that folic acid in daily doses of 10 to 20 mgm. I.M., or 20 to 30 mgm. orally, produced highly satisfactory improvement in the clinical and laboratory picture in pernicious anæmia, the results comparing favourably with those to be expected under adequate liver therapy. The peak reticulocyte responses were generally less than anticipated and were not reliable as an index of the patient's progress.

The evidence at present available suggests that folic acid is not closely related to the extrinsic or intrinsic factors of Castle, nor to the liver anti-pernicious-anæmia factor.

The data on Case 2 are presented through the courtesy of Dr. E. F. Donald.

The synthetic folic acid was kindly supplied by Lederle Laboratories, Pearl River, N.Y.

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The earliest mention of ophthalmology occurs in a law book of Babylon-Assyria in 2250 B.C. Aristotle was the first comparative ophthalmologist. The first textbook on the eye which has come down to our day was written during the first half of the Eleventh Century in Bagdad. Leonardo da Vinci was the first to compare the action of the eye to a camera.—National Health Council.

PERSONALITY CHANGES ASSOCIATED WITH SURGICAL AND RADIATION CASTRATION*

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Essondale, B.C.

THE personality and general adjustment of a woman determine in large measure the severity of her menopause. The specific symptoms of the female climacteric are amenorrhœa and absolute sterility. They are determined by the cessation of ovarian function. Atrophic changes in the genital tract follow and certain systemic symptoms which can be grouped as vasomotor and metabolic, and emotional instability and nervousness, may occur. Sevringhaus states, "Manifestations at the menopause are so varied one is tempted to attribute to the climacteric any complaint without obvious cause".

The chief vasomotor symptom is the "hot flush". McLaren in 1941 in a study of 74 cases of normal menopause (average age 45) found moderate and severe flushing in 16.8%; in 39 simple hysterectomies without oöphorectomy (average age 38) 1.5%; but in 100 radiation castrates (average age 47) this figure rose to 44% and in 39 surgical castrates (hysterectomy and bilateral oöphorectomy) average age 45, 47%. (Symptoms after radiation were in the same proportion in younger and older women). A metabolic upset is suggested by the development of girdle obesity referred to as "middle age spread".

Symptoms of emotional instability and nervousness have been observed by many writers but in the majority of papers no psychiatric study was done and the available data are far from systematic.

McElroy, Snyder and Clark in 1943, in their study of the clinical effects of synthetic œstrogens on the artificial menopause in 42 women report: "The patients who were somewhat neurasthenic and were warned of the side effects of nausea and vomiting promptly developed them after the suggestion of their occurrence was made". Neustaedter in 1943 using premarin, states: "In two instances in which the hormone was not tolerated one patient suffered from nausea and vomiting previous to treatment and the other patient, a surgical castrate, was

* Read before the Psychiatric Section of the Montreal Medico-Chirurgical Society, November 12, 1946.

so unstable that even other medications were of no value''. Hamblen quotes Feldweg to the effect that ''Symptoms following irradiation are not determined primarily by age, but by the patient's basic endocrinologic and psychic pattern — the neurasthenic, psychopathic and mentally unbalanced woman is entirely unsuited for radiation therapy''.

CASE REPORT

Mrs. E.B., aged 54 years, complained of vague general symptoms such as pressure on the head and pain in the back, morbid thoughts, fear of disaster to her family and agitation.

History of present illness.—The patient dates her illness to 1943. In March she was given a radiation menopause for ''chronic metritis with bleeding'', dosage 1,800 mgm. hours; no pathological report. In the summer her husband retired ''on the edge of a nervous breakdown''. She had mild vasomotor symptoms and anxiety, but received no substitution therapy. In August, 1945, her brother died suddenly and her husband collapsed from ''nervous exhaustion'' the day of the funeral. The following winter she was in bed for two months with palpitation, high blood pressure and pain down the left arm. She relied more on ''absent prayer'' than her doctor and quarrelled with her sister at this time. In July, 1946, she developed a fear of travel and nervous indigestion prior to going on a holiday. She became tired and depressed and sleepless and had an obsession that she would have a nervous breakdown. Feelings of imminent disaster and ideas of self accusation developed and she was admitted to the Allan Memorial Institute, Montreal, on September 24, 1946, to the service of Dr. D. Ewan Cameron.

Personal history.—She has always had delicate health and has never gone two years without seeing a doctor. Pneumonia at 2; appendicitis and peritonitis at 11; scarlet fever at 8; curvature of the spine treated by an osteopath at 10; duodenal ulcer 1937 diagnosed by x-ray; ''heart trouble'' 1945. Menses irregular and painful; radiation menopause.

Family history.—Father dead, aged 79. He was domineering and hot tempered. Her mother had a nervous breakdown with depression, at 46.

Summary of physical findings.—(1) Thirteen lb. weight loss in 3 months. (2) Leukoderma over 12 years' duration. (3) Cardiovascular asymptomatic: Pulse 88, blood pressure 198/112. Fundi show no evidence of arteriosclerosis. Special procedures: urine, trace of albumen, blood non-protein nitrogen and brom sulphthalein renal excretion test normal; electrocardiogram negative.

Personality.—Inadequate, dependent, immature emotionally. Hypersensitive, inferiority feelings, youngest child of a neurotic mother, spoiled by relatives. Taught fear by nursemaid. Sheltered life. Poor judgment in business ventures. Married at 43 to a neurotic divorced man, 8 years older. Immature preoccupation with metaphysical religion. Reacts without discrimination to praise. Many non-specific fears and vague obsessions. Has never adjusted to sister's seniority and domineering personality. Worries over money matters, despite financial security.

Mental examination.—Dejected, worried, tense, agitated appearance. Anxious to please, little initiative. Increased psychomotor activity. Circumstantial conversation. Poor inhibition. Stereotyped phrases. Self-accusatory trends. Depression, emotional immaturity and dependency.

Ideas of unreality, self-condemnation and guilt. ''I feel I'm bringing complete disaster on everyone.'' Somatic illusions: pain in back, pressure on head, flooding sensation over body followed by perspiration. Fears: of people in general, of travelling, of going crazy, of being unworthy of her sister and husband. Judgment faulty, subjective insight into depressed condition although not into her personality difficulties.

Diagnosis.—Inadequate personality, with agitated depression and diffuse tension symptoms, phobias and obsessions.

Therapy.—Insulin in somnolent dosage given daily and electro convulsive therapy twice weekly have relieved anxiety, self-depreciation and agitation. Psychotherapy has been started and a prolonged course is contemplated.

DISCUSSION

Psychogenic and somatogenic factors in flushes of the surgical menopause were studied by Reynolds, Kaminester, Foster and Schloss in 1940. Four patients with natural menopause all responded well to œstrogen. Œstrogen alone or combined with phenobarbital was without effect on 10 or 13 castrates, presumably because of neuroses and situational difficulties. The patients' ages varied from 27 to 56 and their symptoms were of 2 months' to 5 years' duration. Brief case histories are given and the authors record that psychogenic factors were elicited only after careful study. One woman whose flushing was under control with œstrogens and was continuing treatment suffered a recurrence of this symptom after she was attacked with a knife by her husband. The authors do not attempt to explain the physiological mechanism. However, they agree with Brew and Davidoff that psychotherapy is of great value where a neurosis is superimposed on the somatic symptoms involved. They pose the question, ''Why does neurosis in the presence of normally functioning ovaries not give rise to vascular disturbances of menopause, but soon after ovarian deprivation, typical vascular symptoms may appear in intense aggravated form?''

Heller and Myers, working with Farney and later with Chandler have correlated menopausal symptoms, vaginal smears and urinary gonadotropins in 27 oöphorectomized women, 23 of whom were subsequently treated with diethylstilbœstrol after the ''menopausal syndrome was firmly established''. Urinary gonadotropins rose significantly between the 6th and 10th postoperative day except in those cases in which the menopausal level had been reached before castration. The menopausal level was reached by 58% by the 6th day and by 86% by the 10th day, 100% by the end of the month. Menopausal symptoms were apparent in all but one case and appeared and reached their maximum severity between the 27th and 66th day. Flushes, nervousness, and sweating were frequent; loss of libido, morning insomnia, arthralgia, palpitation, sweating, vertigo, head-

ache, depression, self-depreciation, crying spells, irritability and fatigue were also recorded. Two patients included here had undergone a spontaneous menopause 3 and 8 years previously. The symptom-free patient had an atrophic uterus and ovaries and high urinary gonadotropin level before operation. Four others whose ovaries were atrophic developed symptoms. Retrogression in vaginal cytology was not correlated with either the gonadropins or the development of symptoms. In the majority, changes in the vaginal smear were not striking. Four controls (a bilateral salpingectomy, a resection of corpus luteum cysts, and two unilateral oöphorectomies) showed normal gonadotropins, normal vaginal smears and no menopausal symptoms.

They conclude that atrophic ovaries should be preserved at operation. Hamblen believes ovarian function in the 45 year old patient must be conserved just as in the 25 year old.

Emotional instability at this epoch has been likened to puberty by Helene Deutsch. It is a time when concealed, repressed and unfulfilled desires are less rigorously controlled and demand expression. Spinsterish, frustrated and frigid women have a stormy menopause. In the interpretation of these changes Heaver cautions: "Should the production of exaggerated affective responses be due to ovarian deficiency, the latter can also be indicted for gross aberrations. Such emphasis entirely neglects the recent and remote personality features namely that she is selfish, has narrow interests, is over-religious, sexually frigid, narcissistic and rigid in social, moral and ethical attitudes". Brew and Davidoff in their study of involutional psychoses found that the prepsychotic personalities were notable for poor integration, poor adaptation and rigidity. At the climacteric, loss of security, inability to face the approach of age and waning aggressiveness led to symptoms of anxiety and guilt.

Precipitants operating to produce symptoms at the climacteric have been listed by Hamblen as follows: (1) fear founded on ignorance of sexual phenomena and dread of the climacteric; (2) sociologic conflicts; (3) domestic infelicity and marital disharmony; (4) financial reverses; (5) improper attention to general health.

Hamblen goes on to include with his precipitating factors some of the early symptoms of lessened stability which have also been described by Deutsch. There is the frigid woman who uses symptoms as a defense mechanism against continued sex relations; the narcissistic woman who is unable to accept the cosmetic alterations of age; the quasihypomanic adjustment of overindulgence in stimulants, too much social activity and inadequate rest and sleep; the hypochondriacal adjustment with its plea for sympathy as a means of retaining the husband's attention. The approach suggested for the mental hygienist is to help the menopausal woman raise her sights from the function of reproduction to the possibilities for self-realization in creative hobbies now those duties are past.

Observations such as have been recorded above lead one to ask whether castration symptoms are due to removal of an organic biological requirement or whether castration alters the individual's conception of herself with resultant production of neurotic symptoms. Until studies of a large number of individuals' personality make-up prior to castration has been done a final answer cannot be given. Hamblen has formulated an explanation of the generally accepted hormonal findings as a four step process.

1. *The ovarian failure phase.* — Œstrogen secretion is reduced progressively at the normal menopause; rapidly if the menopause is artificial. It is not reduced to zero however for œstrin is found in the urine in varying amounts for long periods after cessation of menstruation. However, there is little cyclic alteration in œstrogen formation. The ovary becomes refractory to pituitary gonadotropins. Ovulation and corpus luteum formation do not take place, although the ovaries may continue for a time to respond to the follicle-stimulating hormone.

The phenomenon of flushing accompanies œstrogen diminution and increase of gonadotropins. It can be controlled by administration either of œstrogens or androgens, although when androgens are given to the premenopausal woman, flushing is produced. The work of Heller *et al.* is fairly conclusive in showing that flushing is due to œstrogen withdrawal. Ripley, Shorr and Papanicolaou conclude that the beneficial effect of the œstrogenic hormone in the menopause is confined to the relief of vasomotor symptoms with associated improvement in feelings of well being.

The vaginal smear technique has given the clinician one objective measure of the effectiveness of substitution therapy. Some writers feel that clinical improvement occurs before changes in the vaginal epithelium. In the menopausal woman, Hamblen says that when the vaginal

smear is altered to the reproductive phase, the patient has been overtreated and adds that œstrogens are given unnecessarily to too many climacteric women. McLaren does not feel the vaginal smear is a good index as 84% of his vaginal biopsies were normal before œstrogens. His views were confirmed by Heller.

2. *Pituitary hyperactivity phase.*—A marked increase in urinary gonadotropins is found which Hamblen attributes to compensatory pituitary hyperactivity. Heller found that the ovaries from rats receiving concentrates of post-menopausal urine often showed luteinization as well as follicular growth, and progestational activity was demonstrable in the uteri in instances when the ovaries were luteinized. Heller and his co-workers ascribe the increased gonadotropin excretion to failure of utilization by the ovary. Hamblen believes there is also an increase in thyrotropic and adrenocorticotropic pituitary activity. Heller found that small doses of diethyl stilbœstrol (0.5 mgm. daily by mouth) stimulated the pituitary to produce more LH, although larger doses (5 mgm. daily) suppressed both urinary gonadotropins.

3. *Adrenal and thyroid phase.*—These glands may show secondary hyperactivity depending on the local glandular receptivity and the psychosomatic pattern of the woman.

4. *The adrenal cortical stabilization phase.*—Hamblen found increased amount of steroids are secreted and there is a relative and absolute increase of androgens over œstrogens. Changes in the secretion of cortin-like steroids have not been studied. Bilateral oöphorectomy produces no immediate effect on the urinary 17 ketosteroids. After a latent period of months the level rises to that of primary adrenal cortex hyperactivity and after a lapse of years returns to normal. The adrenal cortex exerts a conditioning influence on the pituitary similar to the previous activity of the ovaries.

In a study of traumatic castration in males, Lange found anxiety symptoms were not greater than in soldiers with other injuries. This finding is in disagreement with Fenichel who emphasizes the symbolic significance of castration to the individual. Bergler and Reich's study of impotence in men disclosed two basic emotional conflicts namely fear of injury and deep seated attachment to parent or sibling.

Pavlov in his studies of experimental neuroses found individual differences in the susceptibilities of the animals to the same morbid agent. The strong animal with weak inhibitory processes and the animal weak in both excitatory and inhibitory elements, but especially the latter, were the most prone to develop neuroses. However, even the strong and well-balanced type could be broken when the morbid agent was intensified, particularly if he had undergone an organic disturbance, for instance, castration.

Certainly the cure of non-specific syndromes such as migraine cannot be expected from the induction of the menopause. Critchley and Ferguson speak of migraine as the happy hunting ground of the theorists for which each branch of medicine has found the infallible remedy. Riley, Brickner and Kurzrok found low urinary œstrogens and a rise of gonadotropins associated with the appearance of a migraine headache. In his survey of 42 cases of women who had migraine and who subsequently underwent oöphorectomy, x-ray or radium castration, Alvarez found 6 were relieved, 5 were milder, 16 unchanged and 15 worse; 3 others suffered their first migraine attack after the menopause. "Particularly the nervous, psychopathic fussy women, especially when they are harassed or overworked, did not improve. One woman became a nervous wreck after hysterectomy was done to cure her headache".

SUMMARY

The case which has been presented illustrates the following features which are said to be characteristic of the menopausal syndrome including the personality disturbances:

1. A prepsychotic personality which was weak and inadequate and showed poor integration. Adaptation was poor even in a sheltered environment. There is rigidity with unwillingness and inability to change her patterns of reaction. Frigidity is also noted which may be related to her strong attachment to her father and later her brother.

2. Radiation castration was performed 3 years ago. The earliest symptom of œstrogen withdrawal was the hot flush which was mild at its onset but after an interval has returned in an atypical form with other symptoms.

3. Precipitants acting to decrease stability have been (*a*) loss of security: concern that husband's symptoms presaged his imminent death, and disillusionment with her religion; (*b*) waning aggressiveness: she has previously

concealed her resentment of her sister's domineering personality, but this hostility has recently been directed against herself and symptoms of anxiety with guilt feelings have appeared.

4. For the patient her symptoms represent a defence against continued sex relations and a plea for sympathy and her husband's attention.

Thanks are due Dr. R. A. Cleghorn for his assistance in the preparation of this paper.

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AURICULAR FLUTTER*

(The Results of Therapy in a General Hospital Over a Ten-Year Period)

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SINCE it was first named by Jolly and Ritchie in 1911, auricular flutter has led a stormy course. Many controversial reports about this entity appeared in the literature for the following twenty-five years and then little was heard of it until the last three or four years when the work of the Californian group with lanatoside C again brought it momentarily into the spotlight.

Most of the statistics dealing with auricular flutter have emanated from noted cardiologists and have had to do with results as achieved by specialists in this field. Accordingly, it was considered worthwhile to make a study of a series of cases of auricular flutter as they occurred in a large general hospital, and to try and evaluate the results of therapy as practised by both specialist and general practitioner alike.

In the ten-year period from 1936 to 1945 there were, in the Vancouver General Hospital, over 13,000 cases whose cardiac signs or symptoms were considered sufficiently important to merit electrocardiography. In this group there were 52 cases of auricular flutter, an incidence of 0.41%, a figure somewhat lower than that found by White[1] at the Massachusetts General Hospital over a similar period. Excluded from our group were many cases of impure flutter-fibrillation, as it was felt that the results of therapy in these cases would interfere markedly with an accurate evaluation. Our age range varied from 22 to 86 years but supported White's observation that three-quarters of the cases of auricular flutter occur after forty years of age. The ratio of males to females was 3:1.

UNDERLYING HEART DISEASE

Our survey showed definitely that auricular flutter is commoner in the presence of heart disease than in its absence. In the table below, the underlying heart diseases are listed with, for comparison, a series of similar size reported by Parkinson and Bedford in 1927. The only significant discrepancy noted is in the number of cases of acute coronary infarction in the two series. This may, perhaps, be explained by the fact that Wolferth and Wood's first paper on the clinical use of precordial leads appeared in 1932, so that some cases of infarction, included in our series, were not so diagnosed before that time.

TABLE I.

Underlying heart disease	*V.G.H.*	*Parkinson and Bedford (1927)*
Arteriosclerosis	17	13
Rheumatic	10	14
Acute coronary infarction	11	3
Hypertension	3	6
Thyrotoxicosis	2	2
Syphilis	2	3
Acute febrile illnesses	1	3
Congenital	..	1
Polyserositis	1	..
No evidence of heart disease	4	5
Total	52	52

In this series of 52 cases there were 12 deaths, and congestive failure was present in a third of the cases, apparently not being directly related to the auricular flutter in the majority of the cases.

* Read before the North Pacific Society of Internal Medicine, Vancouver, B.C., September 7, 1946.

RESULTS OF THERAPY

In evaluating the results of therapy, the cases were divided into three groups:

1. Those who had a return to sinus rhythm as proved by electrocardiography—24 cases.

2. Those who were afforded considerable symptomatic relief but who had no definite return to sinus rhythm—13 cases.

3. Those who were unaffected by therapy—15 cases.

TABLE II.
RESULTS OF THERAPY

Drug	*No. of cases*	*Sinus rhythm*
Digitalis	29	12
(Cedilanid)	(4)	(2)
Quinidine	13	9
Quinidine and digitalis	8	2
No cardiac medication	2	1
Total	52	24

1. *Digitalis.*—The drugs used were both the leaf and tincture of digitalis, digoxin, both intravenously and intramuscularly, digifolin and cedilanid. Sinus rhythm was re-established in 12 of the 29 cases and one very noticeable point was that most of the failures were treated by small, infrequent doses, while all the successes received full, rapid digitalization. The most satisfactory dosage appeared to be 3 to 6 grains of the digitalis leaf or its equivalent every 4 hours until the patient was fully digitalized or until early indication of toxicity appeared. A word might be added at this point about the use of cedilanid or lanatoside C in auricular flutter. Following the method of Sokolow and Chamberlain,[2] 4 patients with auricular flutter were rapidly digitalized in 24 hours with cedilanid used intravenously, usually 6 to 14 c.c. being required. Two of the cases were restored to sinus rhythm, in 24 and 96 hours respectively. The above authors restored 14 of their 17 cases to sinus rhythm, usually within 24 hours. In another case, the auricular flutter was converted to fibrillation which then responded satisfactorily to digitalis leaf by mouth. Tandowsky[3] in his series of cases, effected a marked lowering of his recurrence rate with oral cedilanid but stressed the fact treatment should start with intravenous therapy for an attack. Indications of digitalis intoxication were encountered in 3 of the 29 cases.

2. *Quinidine.*—With the use of quinidine sulphate, sinus rhythm was re-established in 9 of the 13 cases. As with the digitalis preparations, it was noted that the best results were obtained with frequent, heavy dosage. The most satisfactory dosage routine seemed to be, first, a trial dose of 3 grains, then 3 grains every 3 hours and increased by daily stages to as high as 12 grains every three hours or until indications of cinchonism were encountered. This was well illustrated by one case who was treated on separate occasions by two different doctors. The first time he received gradually increasing doses at regular intervals of 3 or 4 hours and responded very satisfactorily. Two years later he received equally large daily doses but given at 6 to 8 hour intervals with no response. He responded immediately when, after a three day rest period, he was put back on a frequent dosage routine. Only one case of the 13 treated developed indications of cinchonism and then only when the dose had been increased to 12 grains every 3 hours. Gold[4] has recommended the use of 10 grains every 2 hours until 30 to 50 grains have been administered. On this dosage he encountered no toxicity to the drug.

3. *Combination of digitalis and quinidine.*—Only 2 of the 8 cases treated thus were restored to sinus rhythm, but this may be attributed to the fact that small, infrequent doses of both drugs were used in the unsatisfactory cases.

4. *No cardiac medication.*—Of the two cases handled thus, one was restored to sinus rhythm. This patient was known to have paroxysmal auricular flutter and his attacks, though fairly frequent, rarely lasted more than one or two days. He was treated prophylactically with 3 grains of quinidine three times a day and had had no further attacks 15 months later.

COMMENT

Hasty examination of the foregoing results might lead one to believe that quinidine was far superior to digitalis in the treatment of auricular flutter. Careful analysis, however, showed that quinidine was used exclusively by specialists who realized the need for large doses. The analysis furthermore revealed that those of the digitalis cases which were treated by specialists had as good therapeutic results as the quinidine cases.

The question of which drug to use first on encountering a fresh case of auricular flutter has given rise to much controversy. Most authors favour a trial of digitalis to begin with, but Gold argues that quinidine should be tried

first since, should it fail, only 24 hours' rest is needed before digitalization can be begun, whereas a longer period is required for the elimination of digitalis.

An important factor which must be kept in mind in attempting to evaluate therapy in these cases is the fact that some of them may be paroxysmal flutter which may reconvert itself to sinus rhythm regardless of treatment. In only 5 of our 52 cases was a history of paroxysmal auricular flutter obtained, but it seems safe to assume that at least a few of the others might belong in this class. Persistent flutter is not incompatible with fair health, provided symptoms and signs of congestive failure are controllable.

CONCLUSIONS

1. Auricular flutter is a rather uncommon cardiac arrhythmia, found most often in males of over 40 years of age and occurring usually in the presence of significant heart disease.

2. In a series of 52 cases treated by both specialists and general practitioners there was confirmed restoration of sinus rhythm in 47%, and significant symptomatic relief in a further 25%.

3. There appeared to be little advantage in the use of either digitalis or quinidine, the important point in the use of both being the necessity for heavy, frequent doses so that the maximum effect of the drug is brought to bear upon the heart in the shortest possible time.

4. The use of rapidly acting, relatively non-toxic glucosides such as lanatoside C or digitaline nativelle should be given a serious trial in restoring a fresh case of auricular flutter to sinus rhythm.

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The personnel of the hospital should be chosen with great care, and the personality of each worker must suit the position he is to fill. Few of us realize how timid and diffident most of our patients are on admission, or how easily they may be hurt by apparent inattention, or frightened by their new surroundings. It is so important to have their reception a cordial and a friendly one, for the first impressions they get of the hospital and of us are often lasting ones. And this is as equally true of the general practitioner's work in his office and in the home as it is of the hospital.—Dr. Donald Guthrie, *The Diplomate*, 12: 89, 1940.

MYOPIA*

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THERE are many false conceptions prevalent about myopia. From surveys and investigations that we have made at the Hospital for Sick Children I believe that myopia is not a disease of the eye but a normal process of development. Babies' eyes are small, particularly in the antero-posterior dimension, but they grow rapidly in the first year of life and then more slowly for the first twenty years. Babies are hyperopic and this diminishes until the average child is normal in the late teens. If the eyeball does not grow enough, hyperopia is present, and if it grows too much the eye is myopic. I believe that the so-called malignant myopia accompanied by staphyloma, choroiditis, and vitreous opacities is a diseased eye, and myopia is a result of the disease and not the cause.

The myopic child should not be considered to have a terrible eye disease and the parents should not be told that it may become blind. True myopia is merely an eye with a refractive error and I cannot agree with those who state that every myopic eye is a diseased eye and the child should be treated as an invalid.

Many ophthalmologists take the attitude that if the child shows signs of myopia, all reading should be stopped, and the child should be taken out of school and put into seclusion for a year, and in 50% of cases they have succeeded in stopping the progress of the myopia. Our figures showed that 70% of cases which were not treated in any way stopped progressing. I believe it is criminal to take a child out of school and have him develop a myopia complex with a fear that he is going blind if he indulges in any sport. What difference does it make if the child wears –2.00 or –4.00? He still has to wear glasses, and the people who do most of the worrying about glasses on a child are those who have never worn them.

That no treatment up to the present time has been successful is borne out by the fact that there are so many types of treatment for

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myopia. Almost every conceivable explanation has been offered as the cause of myopia; heredity, prenatal weakness, the shape of the orbit, overaction of the ciliary muscle, stretching of the choroid, deficiency in the action of the extra-ocular muscles, increase of intra-ocular pressure, pull of gravity on the optic nerve, lack of calcium, lack of vitamins, too much close work, too much light, advance of civilization, and flat feet. There are likely many others, most of which are based on theory and not on actual clinical experience. Some theories have supporters, and others none but the men who suggested them. Many men claim that bad reading habits cause myopia. You all know that children read in the worst possible positions. The child puts the comics on the floor, in a poor light, and reads them with his nose close to the page. But not all these children develop myopia.

A survey of 494 cases of myopia at the Hospital for Sick Children and in private practice was made. For the purpose of this study the cases were divided into two groups: (1) those seen in the eye clinic at the Hospital for Sick Children who were all under the age of fourteen years, refractions in a majority of these cases were followed for at least seven or eight years; and (2) those seen in private practice, who were of all ages.

METHOD OF EXAMINATION

Refraction.—All refractions were done under cycloplegic. Atropine 1%, three times a day for three days was used, up to the age of fourteen in the clinic, and up to the age of ten in private practice. After the age of fourteen homatropine 2%, one drop every ten minutes until six were given, and then at least another twenty minutes allowed before the refraction was started. This appeared to be just as effective as atropine, providing enough was used, and enough time given for it to act. In younger children a retinoscopy alone was done, but as soon as the children were old enough, careful acceptances were done. In the clinic at least two refractionists checked each case. Incidentally, I have found that this element of competition in refraction is an excellent means of making residents good refractionists. Care should be taken not to have the trial frame sit too far out from the eyes. As much as 1.00 diopter difference will be found in the refraction if the lenses of higher power are not put in the same position each time in the frame.

Treatment. — The full correction is given under cycloplegic. Occasionally it is necessary to cut the sphere slightly in the higher brackets if the patient cannot stand normal vision. In our experience it does not seem to make any difference whether the glasses are worn all the time or not. Many girls would rather go around half blind than wear the glasses, and the myopia does not progress. Parents are advised that the glasses can be worn when the child wishes to see at a distance and most certainly should be worn when reading. Bifocals are never prescribed for children because this upsets the convergence-accommodation relationship. Several of our patients had worn bifocals when young and they had great difficulty at university because they had not learned to use their accommodation properly.

No other special type of treatment was given other than ordinary advice about hygiene, good diet, and general pædiatric care. Reading was not restricted, nor were patients asked to stop music or any outdoor activities. They were allowed to lead a normal life.

Results.—According to numerous books and theories these patients should all have become very much worse and developed serious complications, such as choroiditis, uveitis, posterior staphyloma and detached retina, but what did actually happen?

No cases in our series which started at zero or –1.00 when first seen went on to high myopia with fundus changes. There were ten cases that had 9.00 diopters of myopia or more when first seen at the age of two or three years. They all had the typical myopic fundus changes, and it is fair to assume that they were born myopic.

Survey of 243 clinic patients (see Table I).—All these patients were under the age of fourteen years: 33 showed no change in refraction during the years they were followed. There were 60 who showed less than 0.50 diopters of change; 94 showed from 0.50 to 1.00 diopter of change; 32 showed 2.00 dioptres of change (see Table II), and 19 showed 3.00 diopters of change. Two showed 4.00 diopters of change, and 3 showed 5.00 diopters of change. I would like to emphasize the fact that 187 out of 243, or 76% showed less than 1.00 diopter of change over this period. None of these cases showed over 6.00 diopters of change during the

period they were studied. Those with high myopia were high before we ever saw them.

TABLE I.

243 CLINIC CASES—ALL UNDER 14 YEARS OF AGE

Change	*Cases*	*Percentage*
No change	33	13.5
0.0 to 0.50D	60	24.5
0.50 to 1.00D	60	38.5
Total	187	76.5

TABLE II.

Change	*Cases*	*Percentage*
1.00 to 2.00D	32	13.0
2.00 to 3.00D	19	8.0
3.00 to 4.00D	2	1.0
4.00 to 5.00D	3	1.5
None over 6.00D change		
Total	56	23.5

In private practice 251 cases were studied (see Table III): 93 patients showed no change; 18 of these were under the age of fourteen years, 14 were between the age of fourteen and twenty years of age and 61 were over twenty years of age; 68 patients showed less than 0.50 diopters of change (see Table IV); 49 showed from 0.50 to 1.00 diopter of change; 29 showed 2.00 diopters of change and there were only 12 who showed over 3.00 diopters of change during this period. None showed over 6.00 diopters of change in ten years. I would like to emphasize again that 210 cases out of 251 showed less than 1.00 diopter of change. This number is higher than the clinic group because it includes patients of all ages.

TABLE III.

251 PRIVATE CASES—ALL AGES

Change	*Cases*	*Percentage*
No change	93	
Age: Under 14 years	18	19.0
14-20 years	14	15.0
Over 20 years	61	66.0

TABLE IV.

Change	*Cases*	*Percentage*
No change	93	38.0
Less than 0.50D	68	28.0
0.50 to 1.00D	49	16.0
1.00 to 2.00D	29	12.0
2.00 to 3.00D	7	3.0
3.00 to 4.00D	4	2.5
4.00 to 5.00D	1	0.5
Total	251	100.0

To illustrate what I mean about treatment I would like to cite two cases.

The first was a child of eight years of age who on first examination accepted –1.00 sphere. The parents were advised that she might get a little worse and not to allow her to read to excess. Viophate D was prescribed and general eye hygiene outlined. One year later the refraction was –2.00 and she had faithfully carried out the treatment. The patient was not seen again until she was twelve years of age. The parents stated that they had not brought her back because she had been having no trouble. Her refraction was still –2.00. She was now 5 feet 6 inches tall and indulged in all sports and was doing well in school. The mother told us that they had not been able to give her any Viophate D for the last three years, as the child would not take it. She did not like milk, read in the poorest light, at all hours, and was an active athlete. If this child had been given some type of treatment, such as taking her out of school, prohibiting reading, likely a cure would have been claimed.

The second case was that of a university professor, fifty years of age, who saw 20/15 with –10.00 both eyes; there were no fundus changes. He stated that forty years before he had suddenly become very short-sighted and his parents were told that he would go blind, and should be taken out of school. They didn't believe the doctor, fortunately, and put him through the university where he now holds a professorship. The refraction has not changed in twenty-five years. He was very emphatic in stating how grateful he was that his parents had not followed the doctor's advice by putting him in seclusion and semi-invalidism.

Results of blood chemistry investigation.—A group of 30 patients with varying degrees of myopia were studied and blood estimations of calcium, phosphorus, chlorides, phosphatase, and vitamin A and C were done. These were compared with a similar group of patients who did not show myopia. Unfortunately, due to lack of help we were forced to curtail this investigation during the war. It is now being continued and will be reported on at a later date.

CONCLUSIONS

1. Simple myopia is not a disease but purely a refractive error due to the growth of the eyeball.

2. A distinction should be made between simple myopia in which no pathological change in the eyeball takes place, and the diseased eyeball which is accompanied by myopia.

3. The stigma of a diseased eye should be removed from simple myopia and children should be allowed to lead normal lives.

THE ETIOLOGY AND TREATMENT OF HYPEREMESIS GRAVIDARUM

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DISCUSSION of the cause and treatment of hyperemesis gravidarum is as old as Medicine itself. In this communication it is not my purpose to review these, for their number is legion, but rather to review one method of treatment, the administration of adrenal cortex extract, together with comments on more recently discovered adjuvants of therapy, *viz.*, cevitamic and pantothenic acids.

In 1932 I[1] published the case histories of six ambulatory pregnant patients suffering from hyperemesis gravidarum, all of whom were successfully treated by the oral administration of adrenal cortical extract. Other communications[2, 3, 4] summarized the results of 200 patients similarly treated, with 85% success.

In 1937 Freeman and Melick[5] confirmed the foregoing clinical observations, publishing a series of 79 cases treated, with the astoundingly successful ratio of 98% control of symptoms. In 1939 Kotz and Kaufman[6] reviewed the foregoing reports and reported 50 cases of their own. In their opinion "most of the patients were markedly benefited by this form of treatment".

In 1940 Bernstein[7] reported 120 patients treated by the co-administration of suprarenal cortex and vitamin B_1. All of these patients had previously been unsuccessfully treated by other methods. In every instance a marked improvement or complete relief of symptoms occurred within eight days of the institution of treatment.

In addition to the foregoing reports Batteroli,[8, 9] Posalti[10] and Llustin[11] have recorded their observations in the medical press of Argentina, Germany and Spain respectively.

THE ETIOLOGY OF HYPEREMESIS GRAVIDARUM

Immediately following nidation of the human fertilized ovum in the uterus the chorionic placenta commences to secrete increasingly large quantities of chorionic gonadotropin (formerly termed anterior-pituitary-like hormone or prolan) until the sixtieth day, when a peak of 200,000 rat units (Collip) may be produced in 24 hours. The purpose of this high blood titre of gonadotropin is to keep the corpus luteum constantly "whipped up" in order to maintain the minimum progesterone secretion of 10 mgm. daily,[12] so essential to maintain uterine quietude and prevent abortion during the first trimester of pregnancy before the placenta commences to produce progesterone in abundance. From a peak production of as high as 200,000 rat units, measured at the sixtieth day of pregnancy, the chorionic gonadotropin titre of the blood gradually declines until at the ninetieth day it is usually only 5,000 rat units per day, at which level it remains for the balance of gestation.

Coincident with the drop in chorionic gonadotropin titre there is a sudden cessation in the untoward symptoms of "morning sickness" in all pregnant women.

It is postulated that the symptoms of nausea and vomiting, so common in the first trimester of pregnancy, are toxic manifestations of the phenomenally high amount of gonadotropin in the circulation. When this falls at the end of the third trimester symptoms also cease. Some women have gonadotropin titres of only 50,000 rat units per day and in these there may be no symptoms of toxicity.

It is known that the adrenal cortex undergoes hypertrophy in the first trimester of pregnancy, presumably for the purpose of secreting extra cortin necessary for the hepatic detoxication of the excessive quantity of gonadotropin present in the blood stream. When the latter is extremely high a condition of relative cortico-adrenal insufficiency may exist with "morning sickness" manifested as in patients suffering from Addison's disease (regardless of sex). Normal cortico-adrenal function depends upon the presence of at least two vitamins, cevitamic and pantothenic acids. With increasing nausea and vomiting a vicious circle effect of cortico-adrenal and vitamin deficiency occurs which, if not checked, leads to the so-called pernicious vomiting of pregnancy.

TREATMENT OF HYPEREMESIS GRAVIDARUM

The following regimen of dietetic and medicinal prophylactic therapy is recommended for the prevention and remedy of the nausea and vomiting of pregnancy:

At *hora somne* administer the following or some part thereof:

Desiccated adrenal cortex ..... gr. iii to ix
Calcium pantothenate ..... gr. x
One glass of hot lemonade or cold orange or tomato juice.

On awakening in the morning repeat this regimen. Patient to remain in bed *in recumbent position* for ninety minutes when she may have a cup of tea (with sugar but without cream) before assuming the upright position.

Breakfast should consist only of a glass of orange, tomato or grape fruit juice, one slice of lightly buttered toast with marmalade, one or two cups of coffee without cream. (Café au lait is suitable.) Luncheon and dinner are to be normal meals but preceded by a glass of tomato, orange or grapefruit juice or lemonade.

If any symptoms of nausea supervene the nocturnal dose of adrenal cortex should be increased and a suitable dose of the same preparation should be ingested before breakfast, luncheon and dinner.

SUMMARY

1. The etiology of hyperemesis gravidarum is discussed, the high daily production of chorionic gonadotropin being held responsible.
2. Dietary deficiency of vitamins closely associated with cortico-adrenal function, cevitamic and pantothenic acids, are contributing factors.
3. Appropriate treatment is outlined for prevention and cure in ambulatory cases.

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RÉSUMÉ

Le postulat suivant est proposé: les vomissements de la grossesse sont une manifestation toxique dûe à une hypersécrétion des gonadotrophines du chorion pendant le premier trimestre de la grossesse. On sait que pendant ce temps la corticale de la surrénale s'hypertrophie afin de sécréter suffisamment de cortine pour assurer la désintoxication hépatique de l'excès de gonadotrophine: on sait également que la vitamine C et l'acide pantothénique favorisent par leur présence le fonctionnement normal de la corticale de la surrénale. La thérapeutique des vomissements de la grossesse s'inspire de ces données.

JEAN SAUCIER

PSYCHOMOTOR EPILEPSY*

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WHILE the terms idiopathic and symptomatic epilepsy are commonly used without synonyms, as are the terms grand mal and petit mal, it is found when dealing with the other states regarded as epilepsy that many terms are used. It is quite possible that some will object to the term psychomotor epilepsy and would prefer one of the terms such as epileptic variants, psychic epilepsy, epileptic equivalents, dream states, clouded states, masked or larvated epilepsy, or epileptic automatisms. It is with the hope of clarifying our ideas on such states that the following presentation is given. My understanding is that the above given terms are more or less synonymous.

In seeking a definition of the terms the following is that given by Jelliffe and White[1] under the heading of Psychic Epilepsy. "The epileptiform convulsion may be replaced by any one of the many epileptic equivalents". These attacks of "psychic epilepsy" frequently take the form of so-called epileptic automatism or epileptic dream states. In these conditions the patient may do almost anything and when he comes to himself he has *absolutely no recollection* of what has happened. Other manifestations of psychic epilepsy are states of depression, excitement, delirium, stupor, paranoid reaction, etc.

Again, under the heading of epileptic clouded states the same authors say that they are psychotic reactions occurring in epileptics. At times, either preceding or following a convulsive attack, the epileptic may manifest a dazed condition with deep confusion or excitement, anxiety and bewilderment. Associated with this, there may be violent outbreaks, hallucinations, fears, or ecstatic moods with religious exaltation.

For the purpose of the present discussion I am particularly interested in considering whether or not the patient has, following an attack of psychomotor epilepsy, any recollection of what took place. Authorities seem divided in their opinions. Gordon Holmes[2] under the heading of Psychical Equivalents of

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Seizures speaks of them leaving "a complete amnesia". Kraines[3] under the heading of "abortive" or "equivalent" attacks describes actions "for which they have no memory and which they cannot explain".

However, Collier[4] in describing Psychic Fits says that they are "remembered afterwards sometimes in exquisite detail, sometimes only in vague character". Bleuler[5] speaks of a complete or partial amnesia. Hughlings Jackson[6] says "There is not always *loss*, but there is, I believe, always at least *defect* of consciousness co-existing with the over-consciousness ('dreamy state')," and again, "*Loss* of consciousness is not essential for the diagnosis of epilepsy; there may be defect of consciousness only....". Penfield and Erickson[7] under the heading of Dreamy-state Seizures say: "Some hold is preserved on consciousness, or, if not, memory preserves for the patient some record of the state". Wilson under the heading of Consciousness in Epileptic fits says "Some epileptic fits are attended by loss of consciousness, others are not".

The weight of evidence would appear to favour the view that at least some memory of the seizure may occur and it is because of the nature of the cases which I am to describe that I am stressing this point.

CLASSIFICATION OF EPILEPSY

Lennox[9] in speaking of so-called idiopathic or essential epilepsy says that three main patterns stand out, grand mal, petit mal and equivalents. He says that these may be described roughly as (*a*) convulsions (grand mal); (*b*) short lapse of consciousness (petit mal); and (*c*) prolonged period of impairment of consciousness (psychic variant). In referring to the last group he agrees with Wilson and says that these attacks should not be called epileptic equivalents as the "psychic equivalent" is not in fact an *equivalent* but *is* epilepsy. It is not proposed to go into the question of classification further as this simple classification appears to be in fairly general use and serves our purpose. I wish to deal with two cases that I have diagnosed as psychomotor epilepsy, as I believe that cases such as these are not common and it may be that some will question the correctness of the diagnoses.

CASE 1

In September, 1945, a four-year old girl was reported missing and no trace was found of her for about one week. Her body was then found badly mutilated. The thorax and abdomen has been repeatedly stabbed with an awl, the skull had been fractured. A hole had been dug in a garage floor and the body buried in it, after which the earth was covered with some box covers.

Eventually the "crime" was attributed to a boy of twelve years. An extensive search had been organized and this boy had joined the searchers on several nights. Finally, suspicion was directed to the boy but when first questioned by the police he denied all knowledge of the situation. Later that day he asked if anything he might say would blacken his parents' reputation and following this he gave a statement to the police.

The story was gone over several times and the boy did not vary it in the telling. He said that he had been playing with the girl for about ten minutes when a dizzy spell came over him. "The next thing I knew I was choking her. I seemed to be under a spell—just run like a piece of machinery—I couldn't help it when I was doing it. I shook my head and I was O.K. again."

He told of going out of the garage but said that all this seemed to be rather hazy. He remembered that he stumbled over a board, told of going to the basement, returning and picking up a square-nosed shovel. He then dug a hole and remembered covering the body with earth and then with boards. He went to his home and said that at this time he seemed to come out of the haze.

He read the paper, listened to some radio programs and then went to bed and slept "swell". The next morning he described as being the same as any other morning and he had no thought of the child. However, when he heard that she was lost he later said, "I think I knew I done it but I was so scared I didn't tell anyone". He said that he went to the garage almost every night to get wood and would remember about it then but because of his fear he did not tell anyone and he added that overnight he would forget about the incident.

Several nights later when his parents were out he said that a strange feeling came over him. He went out and got a shovel, went to the garage and partly uncovered the body of the child. The feeling again left him and he became frightened. He went down the lane, found some searchers and told them that he had seen some disturbed earth in the garage. It was following this that he gave his story to the police.

The boy was examined by Dr. E. A. Campbell and me about eight days later. He co-operated well, was friendly and gave the impression of being of average intelligence. After having been examined and having told his story he was asked how he had felt since being in detention. He said that he felt fine but was sorry that this had happened. He said that he had cried when first telling of it but that it did not bother him much now. There was no evidence of emotional display when he was examined nor during the time of his trial; actually he seemed somewhat indifferent.

The boy's father was interviewed but was able to add little information other than the fact that the boy had been struck with a car at six years of age. He could give little information about this, however. The boy said that he had not been unconscious, that he remembered getting up and stumbling and says that he started to run home. He was taken to a nearby building for first aid treatment and apparently little more was thought of the accident.

No family history of epilepsy, migraine, asthma, urticaria, nervous or mental disorder could be elicited from the father. The first born child was stillborn, there were two older brothers and two older sisters. He said that the boy got along as well as the other children. His birth and early development, habits, and school record were not remarkable. There was no history of confusion, loss of memory or bedwetting. His teachers appeared to regard him as an average child and he seemed to be well liked. On several intelligence tests done in the school he had done slightly better than average.

Physically, there was little of significance beyond very bad teeth and some enlargement of the thyroid gland. The testes were small and there was no evidence of development of the secondary sexual characteristics.

The fasting blood sugar was 98 mgm. The urine was negative. X-ray examination of the skull was reported as negative.

COMMENTS

Here then was a strange crime. It appeared to lack any motive. The boy stated that he had played with the little girl often and that he liked her. At the time of the trouble he says that he seemed to be "run like a piece of machinery". With what seemed to be a fairly straightforward story from a child who had always been regarded as average and without any apparent motive for such behaviour, a tentative diagnosis of epilepsy was made.

Through the courtesy of Squadron-Leader G. F. Osler arrangements were made to have electrograms done at Shaughnessy Military Hospital.

The first report by Squadron-Leader J. Kershman of the Montreal Neurological Institute gave the following "impression".

"There is clear evidence of pathological cortical discharges originating in the left temporal region. The character of this activity is similar to what is seen in focal epilepsy and on one occasion a burst of activity was recorded resembling a subclinical attack from the left temporal region. Some generalized slow dysrhythmia was also present. The character of this discharge, its location, and the history strongly suggest automatism or ictal epilepsy. In view of the importance of this problem the examination should be repeated for confirmation."

Sixteen days later the examination was repeated. Squadron Leader Osler reported: "There are persistent large amplitude slow waves with occasional sharp waves and bursts of 4.6 sec. activity. Hyperventilation shows a marked increase in abnormalities and within two minutes of hyperventilation breaks into a sustained paroxysmal high amplitude 3/sec. sharp wave activity which persists for nearly a minute following hyperventilation." Impression, diffuse idiopathic epilepsy.

CASE 2

A girl of fifteen years was under observation in the Vancouver General Hospital and was later transferred to the Provincial Mental Hospital at Essondale. I am indebted to Dr. McNair and Dr. Gee of that institution for additional information on her.

This girl had been charged with arson after having set fire to two institutions. Both were totally destroyed at a loss of approximately $165,000.00 It was thought that she may have been responsible for two other fires as well.

The parents were separated and the background of this child was rather doubtful. The patient is said to have suffered a depressed fracture of the left frontal region. The history varied but it is said that she started to have blank spells at twelve to thirteen years of age. There was no aura. She was said to drop articles in her spells. Following these periods she said that she was confused for five to ten minutes and claimed to have bitten her tongue. On one occasion after going to the Provincial Mental Hospital she was observed in a spell in which she appeared to have a lapse of consciousness which lasted five minutes. There were no motor manifestations and no psychic disturbances following.

Her cerebrospinal fluid pressure had been recorded as 232, 244 and 230 mm. on three occasions taken over a seven months' period. Seizures were not brought out by hydration and pitressin. An aerogram was reported as giving the impression of a space-occupying mass arising in the superolateral angle of the right ventricular body and extending across nearly to the mid-line. The neurological examination was reported as negative except for some increase in the tendon jerks of the right leg.

The electrogram was reported as showing continual bursts of 6 per second and 3 per second activity of the type that originates deeply. The area involved was the left temporal region.

This girl had a mental age of approximately 10 years (I.Q. 64). At least one of the fires was started on a dare and one other girl was involved. Nevertheless, in a letter written to her mother there were some interesting comments. "When I get these spells everything turns red for a while. It seems I am not satisfied until I set a fire or see a fire. Here (Girls' Industrial School) I can't do it. It goes away when I try to sleep it off or sometimes it goes away in a few hours. This is what made me light those fires at the institution. I know it because I can remember."

These comments are interesting in the light of Bleuler's[5] remarks. In speaking of *twilight states* he says, "The patients hallucinate . . . among the hallucinations red ones (partly as fire or blood) occur with noticeable frequency".

In this case there was the history of a skull fracture, the record of epileptiform convulsions and the type of electrogram most frequently seen in psychomotor seizures. Are we then, justified in accepting these occurrences as manifestations of epilepsy? I am particularly interested in her comments of everything turning red during a spell and this being followed by a compulsive type of phenomenon.

Many writers[10] say that psychomotor attacks do not occur unless preceded by other attacks such as petit mal, although they agree that these attacks may be overlooked. Bleuler,[5] however, says that *twilight states* most frequently occur post-epileptically but may take place pre-epileptically and instead of the attack (equivalents). He says, "The most frequent are those with an anxious or angry affect which readily lead to brutal acts of violence against the individual himself or others; sexual excitements are the basis of the Ripper murders or frequent exhibitionism. . . . The twilight states leave, in most cases, a partial or complete amnesia."

Bing and Haymaker[10] quote Hughlings Jackson as maintaining that psychic fit always follow an epileptic seizure, which may be so slight and transitory as to escape notice;

furthermore that the milder the attack the more likely the automatism is to be complex and elaborate. Consciousness is dimmed during the attack; very definite depression follows the attack; some patients afflicted react remarkably well to bromide medication.

This view is expressed by Alpers[11] in speaking of psychomotor seizures. He gives the following as evidence for regarding these as epileptic attacks: (1) They are found in patients with other forms of epilepsy with epileptic attacks though they may occur as the only manifestation of seizures. (2) They are associated usually but not always with impairment of consciousness. (3) They are associated with special types of brain waves, six per second. He questions, however, whether or not these are specific for psychomotor seizures. (4) They respond to anti-convulsant drugs, especially dilantin. Lennox[9] disagrees with this latter statement and says that sedative drugs are of little or no assistance in the prevention of attacks.

Gowers[12] in speaking of these seizures says that such automatic action was formerly regarded as constituting the minor attack of epilepsy and was therefore called masked epilepsy (Esquirol) or epilepsia larvata (Morel). He says further that in most cases automatism succeeds a slight attack and is really a post-epileptic phenomenon. It has been ascribed to the temporary failure of the highest centres to control those next below them, which consequently act in an automatic manner. (Anstie, Thompson-Dickson, Hughlings Jackson). He goes on to say that without doubt many crimes have been committed in this state and the point has formed a medico-legal question at many criminal trials.

Further, it is uncertain as to whether such an attack takes the place of a fit, but we are not at present justified in denying the possibility. The patient is often violent and homicidal although perfectly safe in the intervals.

THE NATURE OF EPILEPSY

At this time we might again question the nature of epilepsy. Lennox[9] defines epilepsy as follows: "Recurrent disturbances in the electrical activity of the brain which manifests itself in a symptom-complex of which impairment or loss of consciousness, autonomic nervous manifestations, convulsive movements or psychic disturbances are the essential components. The term epilepsy is non-committant and merely means 'seizure'."

S. A. Kinnier Wilson[8] says that the epileptic fit is nothing else than a symptom; no such disease exists or can possibly exist. Quoting Hughlings Jackson he says, "Speaking figuratively, there is the mad endeavour of the highest centres to develop the maximum of function of every part of the body, and of all parts at once; the phenomena of a very severe epileptic fit show that this endeavour is nearly successful; the patient is almost killed by the paroxysm; and is nearly dead (deeply comatose) after it".

In a later paper on Epileptic Variants Wilson[13] says that "Epileptic possibilities are legion; no rigid semiological framework can be fashioned to embrace them all. . . . The phenomena of the epilepsies edge off by easy graduations from the motor convulsive seizure to psychical, sensory or visceral symptoms of a highly disparate kind." He then classifies the variants as: motor variants; sensory variants; psychical variants; visceral variants.

Penfield and Erickson[7] have defined epilepsy as a state produced by a pathological excessive neuronal discharge within the central nervous system. Brill and Walker[14] discuss psychopathic behaviour with latent epilepsy and point out that in behaviour disorders in children in the Bradley Home 59% of 71 children showed abnormal electrograms. These cases are recorded as having six per second waves and are said to have improved with benzedrine.

COMMENT

The cases described again bring to our attention the necessity for a broad viewpoint on the matter of epilepsy. Peculiar psychotic reactions must be considered, in many instances, as possibly related to epilepsy. However, Gibbs, Gibbs and Lennox have modified the opinion expressed in their article entitled "The Likeness of Cortical Dysrhythmias of Schizophrenia and Epilepsy".[15]

The electroencephalograph is an instrument which definitely supports certain conclusions reached by clinical methods. In this respect it should be regarded as any other laboratory procedure.

No longer is epilepsy accorded the serious prognosis that has been too prevalent. Advances are being made in treatment that bring the condition under control in the great

majority of cases. Further improvement in treatment is promised.[16]

SUMMARY

The question of psychomotor epilepsy is discussed. The retention of the memory of events that took place during the seizure is considered.

Two case reports are included.

The time at which the psychomotor attack occurs in relation to the seizure is discussed.

Comments on the nature of epilepsy are included and the possibility is mentioned of certain mental states and behaviour problems belonging to this group.

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RÉSUMÉ

Les classifications des épilepsies sont encore hésitantes et l'accord universel n'est pas encore fait sur une terminologie qui puisse rallier toutes les opinions. La perte de la conscience ne serait pas essentielle pour signer l'épilepsie. Les renseignements tirés de l'E.E.G. sont importants et ont la valeur d'un symptôme additionnel. L'amnésie peut manquer et certaines phases de la crise peuvent être remémorées. Les phénomènes psycho-moteurs n'ont pas de séquence fixe: ils peuvent survenir avant ou après la crise; ils peuvent parfois remplacer la crise dont ils sont, alors, un équivalent. On n'a pas encore saisi parfaitement la nature intime du syndrôme épileptique dont les mécanismes sont multiples et variés. Il est certain que d'immenses progrès thérapeutiques seront encore accomplis à la lumière des travaux récents.

JEAN SAUCIER

BRUCELLOSIS*

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BRUCELLOSIS is of interest to the physician as undulant fever, a disease which presents problems in diagnosis, control and treatment. It claims the attention of the dairy farmer as Bang's disease, an economic problem which may seriously affect his livelihood. A brief outline of the historical highlights of this very widespread disease may be of interest.

Marston[1] in an Army Medical Report in 1861, gave the first accurate description of the disease in Malta. David Bruce,[2] whose name is perpetuated in the modern terminology of the disease, discovered the causative micro-organism *Brucella melitensis* in the spleen of a fatal case in 1887. Ten years later in Denmark, Bang[3] isolated and studied the bacillus of infectious abortion in cattle now known as *Br. abortus*. Bruce in 1904 headed a Royal Commission in Malta whose investigations proved that undulant fever was milk-borne and existed as a reservoir in goats. The first case of brucellosis was discovered on this continent in 1905 by Craig[4] in a nurse in a hospital in Washington, D.C. The third organism of the brucellosis trio, *Br. suis*, was isolated from a pig fetus in the United States by Traum[5] in 1914.

Alice Evans[6] in 1918, in a classic study showed the inter-relationship of the three brucella organisms to the diseases caused by them in man and animals. Huddleson,[7] working in Michigan, has in the past ten years made many valuable contributions in the field of laboratory diagnostic methods applicable to brucellosis.

The disease is almost world-wide in distribution, being particularly common in agricultural areas. Several thousand cases a year are reported annually from the United States. In 1944[8] there were 226 cases reported in Canada distributed as follows: Nova Scotia 1; Quebec 127; Ontario 55; Manitoba 9; Saskatchewan 4; Alberta 8; British Columbia 22.

These figures probably do not give a true indication of the prevalence of the disease as many cases are not diagnosed.

Brucellosis has a high incidence in cattle throughout Canada. Among 2,713 herds tested

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throughout the Dominion in 1945, 905 showed a positive reaction to blood agglutination tests.[9] In Alberta in 1945 among 4,605 cattle tested 567 gave positive reactions. Among 1,115 dairy cattle tested in the Edmonton district in 1938 Little[10] reported 12% positive reactions.

EPIDEMIOLOGY

Observation over the past 50 years has proved convincingly that brucellosis is contracted by ingesting raw milk or raw milk products such as cheese, butter or ice cream, from infected cows or goats. A less common source of infection is the handling of infected meat or contact with infected cattle, pigs or goats. Moreover infection is believed to occur through the intact skin. Case to case infection has not been reported in man, although living brucella organisms have been demonstrated in the urine in 10% of patients with the disease. One water-borne outbreak has been reported by Newitt as a result of faulty plumbing.

The widespread existence of the disease among dairy cattle and the frequent consumption of raw milk in rural areas makes one wonder why brucellosis is not more common. There is some indication, however, that not all strains of *Br. abortus* are virulent for man. Huddleson[7] has shown that among a group of 500 people of all ages constantly exposed to the ingestion of raw, *Br. abortus* infected milk, less than 1% became infected.

PATHOLOGY

Brucellosis shows a mortality of 3%. Study of autopsy material has given some information as to the morbid anatomical changes produced. The outstanding finding is hyperplasia of the reticulo-endothelial cells of the spleen and lymph nodes. Less commonly areas of necrosis occur. A rare but interesting finding is endocarditis of the aortic and mitral valves.

Culture of autopy material has shown brucella organisms in most of the body organs. This fact is of clinical significance in that active foci of infection may exist in the spleen, lymph nodes, gall bladder and other organs, making for chronicity and resistance to treatment.

IMMUNITY

The problem of immunity to brucellosis presents many difficulties. Experimentally it has not been possible to produce immunity in animals by inoculating them with a suspension of dead organisms. It has been claimed that inoculation of small doses of living brucella organisms into calves has produced immunity to abortus infections. The presence of a high titre of agglutinins in the blood carries no assurance of immunity in man or animal, and strains of brucella organisms seem to differ widely in their antigenicity. It is not uncommon to find positive blood cultures in a sick patient over a period of time without any evidence of serum agglutinins at any stage of the disease. The significance of this finding in evaluating the agglutination test as a diagnostic measure is obvious. Does one attack of undulant fever confer immunity? Bruce from his Malta experience with *Br. melitensis* was convinced that it did. Other observers have stated that second infections may occur. It is generally accepted that children and sexually immature animals are relatively immune.

SYMPTOMS AND SIGNS

The incubation period has wide limits and is said to vary from 5 to 45 days. In practice it is not always easy to recognize the first exposure to ingestion of or contact with the micro-organism.

The onset of the disease is usually insidious with weakness, malaise, anorexia, headache and generalized pains. There is a gradual rise of temperature with evening elevations to 102 to 104° F. and morning remissions. Chills may occur. Sweating is a common symptom. Upper respiratory and digestive symptoms may be noted. The similarity to typhoid fever is striking and will recall to the minds of some of us instances of this now rare disease. As the illness progresses weakness, mental depression, and weight loss may be prominent, but in many cases the patient feels and appears much better than one would expect with the prolonged pyrexia. Physical signs are often conspicuously absent. The spleen is palpable in about a third of cases. A macular eruption is an occasional finding.

The disease runs a varied course. The fever may subside, with subjective improvement at the end of two to four weeks or may continue for as many months. When a remission occurs it may last for seven to ten days only to be followed by a further prolonged period of pyrexia. The typical undulations of fever which gave the disease its name are more common in caprine than bovine infections. Brucellosis may present many clinical patterns, from the asymp-

tomatic latent infection in the ambulatory patient to the acute malignant form with hyperpyrexia leading to the typhoidal state with peripheral vascular failure and death.

COMPLICATIONS

Time does not permit of more than a mere enumeration of the complications of brucellosis. As one might expect the wide dissemination of the organisms in the patient's body leads to many complications. Synovitis and arthritis are of such common occurrence that they might be considered as symptoms. Since brucella infections primarily involve the genital organs of cattle one is not surprised to find that orchitis may occur in man. In the pregnant woman abortion has been reported, but much less commonly than in the pregnant cow. The nervous system frequently bears the brunt of the disease. The high incidence of mental depression creates a differential diagnostic problem from psychoneurosis. Peripheral neuritis is frequently a disabling complication. Two of our patients developed a drop foot.

DIAGNOSIS

In the typical case with a history of exposure to infection the insidious onset with prolonged fever, splenomegaly, leukopenia with positive blood culture or agglutination test the diagnosis is an easy matter. In chronic brucellosis, however, positive objective data either clinical or bacteriological on which to make an indisputable diagnosis are not always available. One has found this precept of value—"If a patient shows a paucity of physical signs and a prolonged fever think of brucellosis".

How much help can we expect from our laboratory colleagues? The leucocyte count is rarely over 5,000 per c.mm. and a relative lymphocytosis is usually present. The blood sedimentation rate is usually normal. Repeated blood cultures may give a growth of brucella organisms. One should be specific in one's request to the bacteriologist as these organisms require special culture media and *Br. abortus* requires an atmosphere of 10% carbon dioxide for growth. A positive serum agglutination test of high titre may settle the diagnosis, but it must be kept in mind that some strains of brucella are weakly antigenic. It is said that in 50 to 85% of cases of chronic brucellosis the agglutination test is negative. The ability of the patient's leucocytes to phagocytose brucella organisms from a smooth culture gives a measure of the patient's response to brucella infection. This test, known as the opsonocytophagic index, gives a quantitative measure of the patient's reaction to the disease. If more than 60% of the cells show phagocytosis one may assume that the patient is recovering from a brucella infection.

An intradermal test using a suspension of killed organisms, brucellin, or brucellergin may be of some diagnostic value. However the skin test here as in suspected tuberculosis has its limitations. A positive test does not indicate an active infection. It is important that the skin tests be deferred until the agglutination tests and opsonocytophagic index have been completed, otherwise the latter two tests may yield false positive results.

DIFFERENTIAL DIAGNOSIS

Brucellosis has to be differentiated from other debilitating diseases with prolonged pyrexia such as typhoid, tularæmia, tuberculosis and influenza. The associated arthritis, in some cases, makes the distinction from infective arthritis necessary. Brucellosis is too often wrongly labelled psychoneurosis because of the prolonged debility existing in the absence of physical signs. Indeed the two conditions may co-exist.

TREATMENT

The multiplicity of therapeutic measures used may be taken as a fair index of the inefficacy of any one of them. Earlier reports indicated that sulfonamides were effective in the acute stages of the disease, but unfortunately they do not prevent relapses. Penicillin is ineffective. The earlier hopes for the efficacy of streptomycin as a therapeutic agent have not materialized. This antibiotic does modify the course of the disease in shortening the duration of the acute attacks, but does not prevent relapses.

The injection of brucellin, a culture filtrate of mixed brucella strains, as a means of producing a systemic allergic reaction with beneficial effect has its advocates. The use of a vaccine of dead brucella organisms over a long period of time is said to prevent relapses. We have had little success with either of these measures.

A few rather dramatic cures have been reported following cholecystectomy and splenectomy in which brucella organisms were recovered from the organs after removal.

Prophylaxis offers a more hopeful approach. Pasteurization is an effective measure for pre-

venting the transmission of the disease by milk and other dairy products. The elimination of positive reactors from dairy herds would help to protect the rural population who drink raw milk. It is still too early to form any opinion as to the value of immunizing calves in helping to stamp out the disease. Veterinarians and others who come into contact with the discharges or tissues of infected animals should be advised to wear rubber gloves. This would hardly be possible in slaughter house workers who frequently contract the disease.

SUMMARY

The history of the development of our knowledge of brucellosis has been outlined.

The disease is common in rural areas and leads to a prolonged disability, with a tendency to febrile relapses.

Brucellosis is characterized by a paucity of physical signs and inconstant serological findings.

While pasteurization of milk is an effective preventive measure we have no specific therapeutic agent for the cure of the disease.

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RÉSUMÉ

L'histoire de la fièvre de Malte, ou brucellose, est passée en revue, aussi bien chez l'homme que chez l'animal. La maladie est fréquente à la campagne où elle tient les malades incapacités très longtemps. Les rechutes sont fréquentes. Cette maladie a une symptômatologie très fruste et les épreuves diagnostiques tirées de la sérologie sont inconstantes. La pasteurisation du lait semble être, à l'heure actuelle, le meilleur mode de prophylaxie. Il n'existe pas encore de thérapeutique spécifique; la streptomycine amoindrit la sévérité de la phase aigue mais elle n'empêche pas les récidives. JEAN SAUCIER

Wise Men Say:

That little men have short tempers.

That it is not work that kills men; it is worry.

That if you and your job are not friends part company.

That the longer you live, if you live right, the less you will think of yourself.

That following the line of least resistance is what makes rivers and men crooked.

That determination reduces hard work to nothing; procrastination makes hard work out of nothing.

That to keep watching, to keep working, to let the brain and hand go together—that is the secret of success. —*Exchange.*

THE TREATMENT OF MOTION SICKNESS

(A Review of Therapeutic Studies Sponsored by the National Research Council of Canada)

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IN the past the treatment of motion sickness has been based in large part on personal experiences of ships' surgeons and other travellers. Often an intense personal interest in the results of the therapy has affected the interpretation of the results. Brochures of manufacturers have added volume to the literature. The large number of drugs enthusiastically recommended for use is mute evidence that such conditions as variability in susceptibility to motion sickness, acclimatization, the physical condition of subjects at the time, roughness of sea or air, psychotherapeutic effects and the enthusiasm of investigators have affected many of the results. In general, the investigations have been poorly controlled and are based on too few experiments. These defects make most of the findings of historical interest only. Although the investigations reported here have been affected by these same factors, their influence has been recognized and efforts have been made to control them (1) by using large numbers of subjects under as standard conditions as possible, and (2) by the consistent use of placebos.

After the fall of France in 1940 it became apparent that invasion would be necessary preliminary to the liberation of Europe. Motion sickness was of grave concern to troops in sea-borne and air-borne operations, and was a definite problem to personnel selected for air crew and coastal naval forces. An evaluation of drugs preventing or alleviating motion sickness was undertaken by groups working under the Associate Committees of Navy and Army Medical Research of the National Research Council of Canada.‡ Other research

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‡ The three Associate Committees of the National Research Council of Canada devoted to medical research for the Services all sponsored studies on motion sickness, which were carried out by the following individuals, Drs. B. P. Babkin, A. Battista, C. H. Best, M. Bornstein, J. R. Brett, B. A. Campbell, A. Cipriani, S. Dworkin, W. S. Fields, J. Howlett, D. H. Jasper, W. H. Johnson, J. Kershman, P. Lehmann, D. Mainland, G. W. Manning, D. McEachern, W. J. McNally, J. C. Meakins, G. Morton, R. L. Noble, J. M. Parker, W. Penfield, M. Schachter, J. W. Scott, E. A. Sellers, N. R. Stephenson, W. A. Stewart, G. Verity, T. E. M. Wardill and C. B. Weld.

groups both within the Services and under the Research Councils of Great Britain and the United States had similar interests, and a free exchange of information with them was facilitated by frequent meetings and by the exchange of progress reports.

Studies were carried out first on the therapy of experimental motion sickness produced in swings, using both animal and human subjects, and, later, in transports and landing craft of various types at sea. An attempt was made to relate the survey of possible therapeutic agents to previous or concurrent investigations of the physiological basis of motion sickness.

Although experimental methods of producing motion sickness had been used previously by several European workers,[39, 45] it was not until the early days of the war that an intensive investigation of experimental motion sickness was started.[7] In 1942 machines which combined horizontal and vertical movements were constructed in the Montreal Neurological Institute and later in the Banting and Best Department of Medical Research in Toronto. Both machines had been designed by Dr. Andre Cipriani and differed only in size. Later, in 1942, they were replaced by simple swings which had been shown to be effective in producing motion sickness, by the workers in England and in the R.C.A.F. Similar experiments, for the most part utilizing simple swings, were later conducted in the United States.

General Procedure

Six swings were installed at H.M.C.S. *York* in Toronto and three at McGill University, Montreal. While a correlation between swing sickness and sea or air sickness could be shown to exist, it did not appear to be of high order. Therefore trials in swings were recognized as preliminary only to those at sea. It was fully realized that even when subjects of proved susceptibility to swing sickness were selected for further therapeutic trials, and when such trials were controlled by placebo treatment, the results of the swing experiments could be used only as an indication of those substances which merited testing at sea. Acclimatization, varying susceptibility to swing sickness, physical condition, activities prior to swinging, age, and experience at sea, were factors complicating the planning of the experiments. With human subjects, the variable protective effects obtained at different times, using the same procedures in the same laboratory, serve to emphasize the difficulties of evaluating drugs used to counteract motion sickness.

The procedure adopted consisted of swinging volunteers from the Canadian Services for a period of one-half hour in order to determine the susceptible individuals. Of the first 3,415 subjects tested, 1,220 (35%) vomited within the half hour and thus gained their selection for further trial. If a drug protected these susceptible individuals against vomiting for 30 minutes it was considered to be effective. Every case had at least one placebo test. An interval of one week elapsed before a subject was used again.

Belladonna Alkaloids

Favourable reports on the use of the belladonna alkaloids in motion sickness had been published by Fischer,[13] Castellani,[9] Blackam,[6] Desnoes,[10] Hill,[17] and others.[23] Some of these authors gave crude belladonna extracts, some atropine, hyoscine or hyoscyamine. One of the well known proprietary preparations consisted of hyoscine and hyoscyamine camphorates. It was considered, however, that further studies under controlled conditions were necessary.

A representative group of figures obtained by the use of some of the belladonna alkaloids is shown in Table I. As can be seen, the percentage of susceptible individuals protected varies from about 40 to 76%. The results obtained by other recent workers agree with these figures. In a few cases higher, and in a few cases lower percentages have been obtained.

Hyoscine appeared to be somewhat more effective than l-hyoscyamine when equal doses were given. Noble's results suggested that hyoscyamine had approximately three-fifths the activity of hyoscine. Parker's figures[35] make it seem likely that the relative activity of l-hyoscyamine is somewhat lower than this. Atropine itself (a mixture of the d and l forms of hyoscyamine) appeared to be less effective than l-hyoscyamine alone. As lævo hyoscyamine is presumed to be more active than the d form in its peripheral autonomic effects, this observation might suggest that this action is more important in preventing swing sickness than that on the central nervous system. The latter action is stated to be exerted equally by the d and the l forms.[14]

A mixture of hyoscine, hyoscyamine and niacin was tested in swing experiments and

TABLE I.

EFFECT OF THERAPY ON SWING SICKNESS

	Mgm.	Number of subjects	% Protection	Reference
Hyoscine HBr.....	0.8	30	76	(35)
	0.75	146	59	(43)
	0.65	30	56	(35)
	0.65	28	50	(29)
	0.4	48	29	(29)
Hyoscyamine HBr.....	1.3	30	52	(11)
	1.0	30	67	(11)
Hyoscyamine camphorate.....	0.8			
plus		75	50	(11)
Hyoscine camphorate..	0.2			
Hyoscyamine HBr.....	0.6			
plus		35	46	
Hyoscine HBr.....	0.16			
"	0.16	34	55	
Hyoscyamine HBr.....	0.8			
plus		30	60	(35)
Hyoscine HBr.....	0.3			
"	0.3	23	64	
"	0.3	22	64	
"	0.3	20	40	
"	0.3	10	60	
"	0.3	30	67	
Atropine sulphate.....	0.6			
plus		35	14	
Benzedrine sulphate...	10.0			
Atropine sulphate.....	1.2			
plus		10	20	
Benzedrine sulphate...	10.0			
Hyoscyamine HBr.....	0.9			
plus				
Hyoscine HBr.....	0.024	44	59	(11)
plus				
Atropine sulphate.....	0.074			
"	0.074	30	80	(11)
Atropine sulphate.....	1.2			
plus		21	29	(11)
Hyoscine HBr.....	0.16			

gave very promising results. This finding was confirmed in sea trials. (In many cases niacin caused a flushing of the face which may have produced a favourable psychotherapeutic effect. This effect was not duplicated by the placebos). Later results in swings (Noble,[29] Parker[35]) and at sea showed, however, that niacin did not increase the protection given by the hyoscine-hyoscyamine mixture alone.

TOXICITY AND DOSAGE

As has been indicated, the protective effect of the belladonna group is a function of the dose given, within certain limits. Quite clearly a therapeutic agent with undesirable side effects would be of little value. In the case of barbiturates or other hypnotics, narcosis was the principal contraindication.

The belladonna alkaloids have produced three types of side effects. The first of these, an action on the central nervous system producing hallucinations, an excited state, or more commonly a mental "cloudiness", was regarded with the greatest concern. It occurs most prominently with the use of hyoscine. While Lomholt[20] has pointed out that hyoscine can be given safely in large doses (3 to 4 mgm. per os) and that in 30 subjects who received such doses only 2 showed mild hallucinations, it was found in the Canadian investigations that the sensation of "cloudiness" is common with doses of from 0.8 to 1.2 mgm. Peripheral manifestations such as a change in heart rate, dry mouth and cessation of sweating, may also occur at this dosage level. A dose sufficient to produce ocular symptoms, especially a disturbance in near vision, was considered unsuitable for use in a motion sickness remedy. When hyoscine hydrobromide (1.2 mgm.) was administered repeatedly, in addition to a dryness of the mouth and some disturbance of near vision, some subjects complained of the unpleasant mental effects noted above. When hyoscyamine hydrobromide was used, similar doses could be administered with impunity. While a dry mouth, or even occasional visual disturbances resulted, the effect on the higher centres was definitely less.

In view of the undesirable effects of large doses of hyoscine it was considered advisable to keep the amount as low as possible and to increase the therapeutic effect by adding hyoscyamine. In one experiment Sellers[41] administered a mixture of 0.8 mgm. hyoscyamine and 0.3 mgm. hyoscine to 57 healthy young adults at 10-hour intervals for 40 hours giving the full amount the first dose and one-half quantities thereafter. Tests for near and far visual disturbances and accommodation were performed. No adverse symptoms were noted after the first dose. While from 40 to 50% of the subjects complained of a dry mouth after the four doses only one showed any evidence of visual disturbance. Other complaints were no more frequent than those in a control group. There was no evidence of cycloplegia. In the dosage recommended no ill effects were noted in physical or mental performance. The diminution in sweating produced by this amount of belladonna did not contraindicate its use in hot climates (H.M.T.[18]; Scott[42]). As can be

seen from the table, a mixture of hyoscyamine hydrobromide 0.8 mgm. plus hyoscine 0.3 mgm. gives protection against swing sickness of the same order as 0.8 mgm. of hyoscine. Since the side effects of this mixture seemed less objectionable than those of an equivalent amount of hyoscine hydrobromide alone, it was considered suitable for trial at sea.

BARBITURATES

This section of the report concerns the treatment of motion sickness with various barbiturates and gives the details of some of the investigations. Reports from other countries are listed, but are only discussed when the results are relevant to the Canadian work which is being reviewed. Sedatives have been used in the treatment of sea sickness for many years and various barbiturates have been recommended. When the search for new drugs was initiated in 1942 it seemed possible that certain compounds might possess a specific depressant action on the higher centres concerned in vomiting. The barbituric acid derivatives were therefore of interest since so many possessed a central hypnotic action, and it was possible that some might cause specific depression of the vomiting mechanism without giving rise to any side effects.[27] From the experimental results which have been obtained it appears that the property of preventing motion sickness is possessed by many barbiturates, but is not necessarily related to the hypnotic or anæsthetic potency of the compound. This summary will refer briefly to a number of compounds which have been investigated, but more fully to one drug designated V-12 (ethyl β-methyl-allyl thiobarbituric acid)* which has shown promise as a therapeutic agent.

Barbiturates as well as numerous other drugs have previously been reported as effective treatment against sea sickness, and the evidence has been given by McEachern, Morton and Lehman[23] in their comprehensive review. In 1932 Hamilton[15] reported observations upon some 400 individuals, and concluded that sodium amytal is more effective than hyoscine or barbital. McLaughlin[24] treated 55 cases of sea sickness with sodium pentobarbital, 100 mgm. on embarkation and thereafter 30 mgm. three times daily. He reported improvement in 88% of the cases. Hill[17] noted that barbital, phenobarbital and amytal, either as the acid or sodium salt, were effective therapy in certain cases. Holling, McArdle and Trotter[18] found that phenobarbital gave slight protection against sea sickness, but was not as effective as hyoscine. Recent experimental results obtained with bromides and bulbocapnine have been described by Babkin, Dworkin and Schachter.[2]

* Supplied by Abbott Laboratories.

MOTION SICKNESS IN DOGS

A large number of barbituric acid derivatives or closely related compounds have been studied in the prevention of motion sickness in dogs (Noble[26]). From these observations it may be concluded that the great majority of such drugs can effectively prevent swing sickness in susceptible animals and in many cases the effective dose does not give rise to any untoward symptoms. The effect is prolonged and is not necessarily related to the sedative action of the compound. Many of the effective compounds which appeared from animal study to be suitable for human use were, for purposes of secrecy, given a number and the prefix "V". It is not possible here to enumerate all the tested compounds, but the effect of V-12, ethyl β-methyl-allyl thiobarbituric acid may be cited.

This compound was given by mouth to a group of 16 susceptible dogs and was found to prevent swing sickness in every animal. The doses required were from 1.25 to 30 mgm. per kg. body weight, and were directly related to the previously determined degree of susceptibility of the animals (Noble[27]). In these experiments no serious side effects were noted, although with the largest dose some animals became mildly ataxic. Comparative tests on the dogs with sodium ethyl iso-amyl barbiturate (amytal) showed that this drug was very slightly more effective than V-12. Of some of the more commonly used sedatives the order of activity on motion sickness was: sodium ethyl n-butyl barbituric acid (neonal); sodium ethyl (1-methyl-butyl) barbituric acid (nembutal, pentobarbital); sodium ethyl phenyl barbituric acid (phenobarbital, luminal); sodium diethyl phenyl barbituric acid (barbital, veronal).

The first two compounds were of the same order of activity as amytal and V-12, whereas barbital was only half as active (Noble[28]). Although all these compounds were relatively active, it may be pointed out that they were not the most potent, since, for example, ethyl 1:3-dimethyl-butyl barbituric acid was from two

to three times more active than V-12 on a weight basis, and even the most susceptible animals were protected by a dose of approximately 5 to 10 mgm. per kg. Toxicity studies unfortunately did not warrant human trials with this compound (Noble[26]). It is of interest to note that atropine, hyoscine and hyoscyamine are totally inactive in preventing motion sickness in dogs (Babkin and Dworkin,[1] Noble[29]).

TOXICITY STUDIES

The toxicity data which will be summarized here concern only V-12. Reports of the side effects of a number of other barbiturates have been made (Noble[30]).

Adult rats (fasted 18 hours or fed) were given V-12 in alkaline solution or as the acid in suspension by stomach tube. In fasted rats a single dose of 50 or 100 mgm./kg. produced no deaths although symptoms were present with the larger dose; 150 mgm./kg. gave a 75% mortality. In fed rats 200 mgm./kg. gave 50% mortality. With the V-12 acid suspension in fasted rats 300 mgm./kg. caused 37% mortality. The effect in rats was depression associated with severe spontaneous muscular contractions, twitchings and convulsions, typical of certain barbiturates. The symptoms started within a few minutes after administration in fasted animals, and complete recovery did not take place for 36 hours or longer in some cases (Noble[31]). These effects were confirmed by Richards.[40]

In mice the effects of daily subcutaneous injections of V-12 have been studied. With doses of 120 mgm./kg. or more, all the animals died within 30 days, and with doses of 60 mgm./kg. or less the mortality varied from 0 to 50%. Muscular twitchings and convulsions resulted when the dose was 100 mgm./kg. or more (Parker[35]).

In dogs different effects of repeated doses have been reported. In one experiment, doses of 5, 10, 15 and 20 mgm./kg. given orally for six out of every seven days for 30 days did not give rise to any symptoms in 7 dogs. A single dose of 50 mgm./kg. caused severe ataxia for 8 hours with complete recovery in 18 hours. A large number of animals received single doses under 30 mgm./kg. in swing experiments without any adverse effect. With 30 mgm./kg. about half the dogs showed mild transitory ataxia (Noble[31]). Richards[40] in toxicity studies in dogs, found that a single dose of 25 or 50 mgm./kg. caused some ataxia. Transitory hypnosis was seen with larger doses. When a daily dose of 25 or 35 mgm./kg. of V-12 powder was given in food to 4 dogs and continued for 24 days the animals remained normal throughout, without depression or ataxia. Hæmoglobin, red and white blood counts and plasma protein remained unchanged. At autopsy only minor changes were noted. In Parker's[35] study however, some of the dogs which received 10 mgm./kg. daily died, but at autopsy the cause of death was apparently pneumonia. Histological examination of the livers of mice and dogs receiving 40 mgm./kg. or over showed varying degrees of degeneration and the type of damage characteristic of thiobarbiturates.[35] It would appear therefore that V-12 in effective dosage has only mild toxic properties but is probably slowly cumulative and may in large doses cause liver damage.

Twenty human subjects received V-12, 190 mgm. or 315 mgm., plus belladonna alkaloids, daily for 30 days. These cases showed no symptoms, and liver function tests were normal throughout. Even the larger dose of V-12 was not an effective sedative for restless patients (Parker[35]). The structural similarity of V-12 and diethyl thiobarbituric acid would suggest that there is a potential danger of causing agranulocytosis when V-12 is used but no cases have been observed. In other experiments it appeared that 315 mgm. as a single or divided daily dose is well tolerated; only a small number of more sensitive subjects may feel slightly drowsy. With a divided dose of 460 mgm. in a day some degree of sleepiness is normally present, but it is not extreme. Doses up to 630 mgm. have not caused symptoms of muscular twitching in human subjects. The use of the acid rather than the more soluble sodium or calcium salt, and the taking of the drug with a meal, seem to reduce the hypnotic effect. Tests conducted by Tyler[46] with V-12 showed that a single dose of 250 mgm. did not have any adverse effect on marksmanship in rapid rifle fire up to 3 hours after taking the drug. He found also that M.S.P. (motion sickness preventive) Army Development Type U.S., a mixture containing sodium amytal, atropine and hyoscine, was well tolerated.

TREATMENT OF SWING SICKNESS IN HUMAN SUBJECTS

Reports from a number of groups of workers have been made on the therapeutic effect of various barbiturates on motion sickness induced by swinging. In reviewing these, considerable variation in results is apparent, and direct comparison of the findings is misleading. The types of swings, the degree of swinging, the criteria of susceptibility and of protection have not been uniform. A summary of the different methods has been made by Campbell.[8] The first barbiturate in Noble's series which animal results indicated to be worthy of trial was V-1, ethyl allyl thiobarbituric acid (Noble[32]). It was investigated in human subjects by Fields, Campbell and Penfield,[11, 12] and was found to be quite effective against motion sickness, but the dosage required gave rise to objectionable toxic effects. These included disorientation, amnesia and excitement. Furthermore, in these experiments various belladonna mixtures were more effective than V-1 and were not toxic.

Subsequently a number of barbiturates relatively effective in dogs but with low toxicity, were tested on humans. These include: V-5—ethyl (1-methyl-butyl) thiobarbituric acid

(pentothal); V-7—ethyl iso-amyl thiobarbituric acid (thioethamyl); V-8—ethyl n-butyl thiobarbituric acid; V-9—n-butyl (1-methyl-allyl) thiobarbituric acid (somalbutyl). In general these were found to have little protective action, even when the largest tolerated doses were used. These results have been reported by Parker, Sellers and Stephenson,[38] Parker, Fields and Sellers,[36] and by Noble.[29] Di-ethyl barbituric acid has also been reported as inactive by Hemmingway and Smith.[16]

Certain thiobarbiturates act as convulsants in high dosage, and have little hypnotic effect in small doses. One of these, V-12, has a protective action in dogs and was first shown to be effective in human subjects by Battista, Bornstein and Noble[5] in swing experiments. The results of more extensive trials with this and other drugs have been published by Noble.[29] In these tests V-12 in a dose of 315 mgm. was found to be more effective than the barbiturates listed below:

V-14 ethyl crotyl thiobarbituric acid	130 mgm.
V-15 allyl sec.-butyl barbituric acid	65 mgm.
V-16 dicrotyl barbituric acid	190 mgm.
V-17 allyl isoamyl barbituric acid	130 mgm.
ethyl isoamyl barbituric acid (amytal)	65 mgm.

It also appeared more effective than various belladonna mixtures. On the other hand Parker[35] did not find V-12, 315 mgm. as effective as hyoscine HBr in 0.8 mgm., or a hyoscine HBr 0.3 mgm. hyoscamine HBr 0.8 mgm. mixture. In the first experiments V-12 was given in divided doses whereas in the latter case a single dose was used. Some individuals were found who responded to V-12 and not to belladonna alkaloids, while in others the reverse was true. In most cases which responded to treatment, either form of therapy was successful. Noble[29] also found that when V-12 was given in addition to hyoscine, or hyoscine and hyoscyamine a greater degree of protection resulted. Parker,[35] and Smith,[44a] however, did not find that this mixture was any more effective than hyoscine alone.

SEA TRIALS

Extensive trials at sea were carried out from the United Kingdom, the United States and Canada. In spite of the difficulties of organization and an astonishing lack of rough weather at the right time, the final results obtained in different trials agree remarkably well. Certain facts learned in the swing experiments proved helpful in conducting the sea trials. Assumption of the supine position materially decreased the incidence of sickness in swings[14, 19] and at sea.[18] In transports this factor was troublesome as subjects could not be supervised at all times by the limited number of observers available.

The necessity of referring results of treatment to the protection rate afforded by placebos was also appreciated. In all sea trials definite protection (of the order 20 to 30%) was afforded by placebo treatment as compared with untreated groups.[21]* In the trials it was usually only possible to study the effect of a single administration of the drug. With repeated doses the results appeared to be more variable.

The first trials were reported from England. These were carried out in coastal landing craft by Holling, McArdle and Trotter[18] who concluded that hyoscine HBr 0.6 mgm. was the most generally useful drug. With this drug from 50 to 75% of susceptible individuals were protected, as compared with an untreated group.[1] In higher dosage greater protection was afforded.

In trials carried out in troop transports (large passenger liners) it was found that hyoscine HBr 0.3 mgm., hyoscyamine HBr 0.8 mgm. and niacin 100 mgm., with the addition of the barbiturate V-9, gave a significant degree of protection (4% ill), over a placebo-treated group (10.1% ill): 220 subjects were in each group. Without the barbiturate the protection observed was essentially similar, 6% against 12.5% in groups of 160 and 200 respectively. In an untreated group of 211, 28.4% of the subjects became seasick.[29]

Additional trials were carried out in the United States. The first of these was a co-operative venture directed by Surgeon-Captain Best, in which members of the U.S. and Canadian Research Councils, as well as U.S. and Canadian Naval personnel took part. L.S.T.'s carrying troops as passengers were used in the experiments.

The results were analyzed and reported by Luykx,[21] who found that a significant degree of protection over a placebo was given by hyoscine HBr 0.6 mgm.; hyoscine HBr 0.3 mgm., hyoscyamine HBr 0.8 mgm., niacin 100 mgm.; and hyoscine HBr 0.4 mgm., atropine sulphate

* Tyler[48] has stated that placebos were without effect in some of his sea trials. This was certainly not the Canadian experience.

0.3 mgm., sodium amytal 130 mgm. But no one remedy was significantly better than another.

A continuation of the tests, carried out in California by Tyler,[46, 47, 48] consisted of ship-to-shore landing operations with brief exposure to motion. The following remedies were tested:

M.S.P. (motion sickness preventive, Army Development Type)—Hyoscine HBr 0.4 mgm., atropine sulphate 0.3 mgm., sodium amytal 130 mgm.
R.C.N. (Royal Canadian Navy): Hyoscine HBr 0.3 mgm., hyoscyamine HBr 0.8 mgm., nicotinic acid 150 mgm.
Hyoscine HBr: 0.6 mgm.
V-12: 250, 325, 375 mgm.
V-12: 250 or 325 mgm. + hyoscine HBr 0.6 mgm.
V-12: 250 or 325 mgm. + hyoscine HBr 0.3 mgm., hyoscyamine HBr 0.8 mgm.

This large series (of more than 15,000 tests) was examined by Merrell,[25] who concluded "that the illness rate on drug therapy is approximately 40% of the placebo rate. There is no evidence that any one of the first three remedies is more effective than another. There is some indication that the three remedies involving V-12 were less effective than the others, but this difference is of a very low order". Barrow, Conn and Williams[3] had previously found M.S.P. effective in trials at sea. Only brief reports on the treatment of air sickness by barbiturates are available from the Office of the Surgeon General, H.Q. Airborne Command, U.S.A.[34] In the tests reported, neither M.S.P. nor hyoscine HBr 0.65 mgm. were effective in preventing air sickness. In another report by Smith[43] these drugs afforded some protection in tests carried out at Randolph Field. Hyoscine HBr 0.8 mgm. gave definite protection.

SUMMARY

Belladonna alkaloids.—The use of belladonna or its alkaloids in combating motion sickness appears to be well founded. Although hyoscine is probably the most effective single drug used in therapy, there is reason to believe that a hyoscine, hyoscyamine mixture may be given with less danger of unpleasant or dangerous side effects than an equivalent dose of hyoscine alone.

Tolerance to belladonna alkaloids varies among individuals. In healthy young men of average size (70 kg.) it has been found that an initial dose of 0.3 mgm. hyoscine HBr plus 0.8 mgm. hyoscyamine HBr is effective, and apart from causing a dry mouth produced no adverse effects. The protection lasts for from 6 to 10 hours. Subsequent doses should not be more than one-half the initial one, and should be separated by an interval of 8 hours or more. The presence of a dry mouth is not regarded as a contraindication to further treatment. It should be remembered that the tolerance of children to belladonna is lower than that of adults.

Therapy with V-12 alone.—From a consideration of the recorded data it would seem justified to conclude that some barbiturates exert a protective action against motion sickness. V-12 while possessing as good, or better protective properties than most barbiturates, has such a low depressant action that doses of 315 mgm. or more can be tolerated without undesirable side effects. For this reason it would seem on the basis of the swing experiments to be a useful compound for the treatment of motion sickness. There is considerable individual variation in the effective dosage. According to Noble[33] the best results, when V-12 is used alone, appear to be obtained if therapy is started the day before exposure to motion. Divided doses seem preferable, and very few individuals have shown undesirable symptoms when 155 mgm. has been been taken with breakfast and 155 mgm. with supper. Taking V-12 with a meal appears to be desirable, presumably because absorption is prolonged. Whereas many cases have been protected by such therapy it is possible to increase the total dose in resistant individuals. An extra 155 mgm. may be taken with the mid-day meal. Therapy should continue during short trips, but the duration of protection after the drug is stopped is probably 15 to 18 hours. The immediate symptom of overdosage is sleepiness, and this symptom should be used in assessing the tolerance of an individual. In some cases this may be a desirable feature, but it should definitely contraindicate any increase in dose. In no case should a total of more than 460 mgm. daily be used. In cases requiring a dose as large as 460 mgm., a reduction after 1 or 2 days is advisable.

Where prolonged therapy is necessary it should be clearly recognized that thiobarbiturates in large doses experimentally may cause liver damage and certain compounds closely related to V-12 have been followed by the sudden onset of fever and agranulocytosis. Since detoxification of V-12 probably takes place in the liver, any impairment of function of this organ would be a contraindication to its use.

Mixture of hyoscine, hyoscyamine and V-12.—In the preceding pages dosages of the belladonna alkaloids or of V-12 have been sug-

gested. The evidence is conflicting regarding the effect of adding V-12 to the belladonna alkaloids. Attempts to make sea trials, using large numbers of subjects, further to test this point were "ruined by fair weather". It is unlikely that a carefully controlled study at sea will be possible under peace-time conditions. In view, however, of (1) the absence of toxicity of the mixture when given over a prolonged period to human subjects (Parker[35]); (2) the greater duration of action of V-12 than that of the belladonna alkaloids; (3) the evidence (Noble[29]) that certain individuals respond to V-12 but not to the alkaloids and vice versa; and (4) the results of the Canadian trials which indicate this mixture to be *at least* as effective as any other which has been tested, it has been decided by the National Research Council of Canada, on the advice of Medical Committees interested in this field, to recommend the following mixture to the Canadian Armed Services:

Hyoscine HBr	0.1 mgm.
Hyoscyamine HBr	0.3 mgm.
Ethyl β-methyl allyl thiobarbituric acid (V-12)	130.0 mgm. (2 gr.)

This mixture has been termed the Canadian Motion Sickness Remedy — National Research Council Formula. The dose suggested is 2 capsules taken two to four hours before exposure to motion. Further treatment should be one capsule every eight to twelve hours. Individuals who are very susceptible to motion sickness may receive increased benefit if therapy is started twenty-four hours before exposure to motion. Undue hypnosis, dryness of the mouth, etc., should be promptly followed by reduction in dosage. In no case should more than 3 capsules be taken within twenty-four hours. In small adults or children the dosage should be reduced. To prevent undue accumulation of the thiobarbiturate treatment should never be given for more than five days each week.

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In this country (England), in the reign of Charles II, Dr. Jonathan Goddard obtained 5,000 for disclosing his secret for making a medicine called *"Guttæ Anglicanæ"*. And in 1739 the Parliament of England voted 5,000 to Mrs. Stevens for a solvent for stone; notwithstanding which there have been as many human calculi since formed by his majesty's liege lithotomical subjects as would macadamize one side of Lincoln's Inn Fields. The celebrated David Hartley was very instrumental in procuring this grant to Joanna Stevens. He obtained also a private subscription to the amount of 1,356, published one hundred and fifty-five *successful cases*, and, by way of climax to the whole, after eating *two hundred pounds weight* of soap David himself died of the stone!—William Wadd, Mems., Maxims, and Memoirs, London, 1827.

CASE REPORTS

SARCOMA OF THE PROSTATE

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Sarcoma of the prostate is a comparatively rare condition. The first case was reported in London in 1839 by Stafford,[3] and since that time about 150 to 200 cases have been reported. It must be remembered that according to Ewing[1] many of these reported cases were probably metaplastic or anaplastic carcinomata, and probably some were the result of constitutional dyscrasia such as leukæmia. Here at the Royal Victoria Hospital we have had only two cases in 16,499 male urological admissions during the past 29 years (1917 to June, 1946). There were 2,418 cases operated on for vesical neck obstruction. There were 384 proved cases of carcinoma of the prostate, and 2,032 cases of benign prostatism, that is, a ratio of 1:5.3. The two cases of sarcoma of the prostate in 386 malignancies therefore represent about ½ of 1% of prostatic malignancy.

In 1943 Melicow, Pelton, and Fish[3] published a comprehensive report reviewing the literature up to that time. The literature as shown by them is extensive, more than 137 reports being published on this rare disease. A few months later Kirschbaum, Larkin, and Culver[2] reviewed the lymphosarcomas of the prostate up to that time, and added another case of their own.

The following is a résumé of the pertinent facts about sarcoma of the prostate brought out in the excellent article by Melicow *et al.* mentioned above.

The etiology is unknown. This malignancy is of mesodermal origin, and arises from the prostatic elements other than the glandular, namely, smooth and striated muscle, fibrous tissue, interstitial lymphoid foci, and vascular elements. This sarcoma has been reported in all age groups, but is chiefly a disease of youth. The reported cases include 19 different types such as round and spindle cell sarcomas, fibrosarcoma, myxosarcoma, lymphosarcoma, leiomyosarcoma, etc. These tumours are rapidly growing, infiltrate locally, and metastasize widely.

The symptoms are those of any vesical neck obstruction, namely, frequency, nocturia, and difficulty in voiding. Pain is usually absent, but was an early symptom in both cases being reported here. The growth may compress and distort the posterior urethra, causing narrowing of the urinary stream with burning and retention. It may extend anteriorly and form a palpable abdominal mass. It may extend posteriorly and encroach upon and compress the rectum giving rectal symptoms. The extension may occur to the perineum and simulate a perineal abscess as in one of our cases.

The diagnosis is usually made at operation or autopsy. Sarcoma of the prostate should be ruled out in any male under 40 years of age with symptoms of vesical neck obstruction and an enlarged prostate per rectum. The differential diagnosis includes: benign hypertrophy of the prostate, prostatic abscess, carcinoma of the prostate, tuberculous prostatitis, cyst of the prostate, cyst of the seminal vesicles, carcinoma of the bladder.

The prostate per rectum is enlarged and usually soft and boggy, and may or may not be tender. The serum acid and alkaline phosphatase are not elevated. The prognosis is poor. The treatment consists of deep x-ray therapy. Surgical intervention is advised only for the relief of bladder or bowel obstruction.

CASE 1

L.A., a 17-year old white male was admitted to the urological service of the Royal Victoria Hospital October 24, 1933, for investigation. His complaints were: (1) increasing urinary frequency during the day with nocturia for the past 2 months; (2) aching pain in the left thigh and leg, 3 weeks, worse during the past week; (3) difficulty in starting the urinary stream and some pain in voiding, 2 weeks; (4) pain over the left sacroiliac region, 2 days.

Past history.—There was no history of hæmaturia, nor of any urological complaints prior to the present illness. Family history was non-contributory.

Physical examination.—Poorly nourished and developed white male youth, not in any acute distress. Heart and lungs were clear; blood pressure 108/62. The extremities appeared normal, there was no muscle wasting, no joint swelling or tenderness. All joints moved freely and well. There was no costo-lumbar tenderness, and neither kidney was palpable. The bladder was not distended. The urethral meatus was clean, and there was no discharge present. The foreskin had been circumcised, there were no penile scars. The scrotum and contents were normal. The prostate per rectum was enlarged, especially the left lobe which felt boggy; the right lobe felt tense.

A No. F. 14 soft rubber catheter was introduced into the bladder, and was held very snugly by the prostatic urethra. The residual urine was 30 c.c. Urinalysis was negative. Phenolsulphonphthalein excretion for 2 hours was 80%. Hgb. was 75%; leucocyte count, 10,800 per c.mm. Blood non-protein nitrogen 21.5 mgm. %; creatinine 1.2 mgm. %. The blood and spinal fluid

Wassermann tests were negative. Chest x-ray showed an essentially healthy chest.

Plain film of the pelvic region on October 30 showed no abnormal shadows, and no bone changes. Film with 10 ounces of 10% NaI in the bladder (Fig. 1) showed a deformed bladder outline with marked intrusion on and elevation of the floor of the bladder. On November 3, cystoscopy was performed under spinal anæsthesia. Cystoscope F. 24 introduced with some difficulty, meeting an obstruction in the prostatic urethra. The prostatic urethra was elongated. The bladder mucosa appeared normal, no marked intravesical prostatic intrusion. Retrograde pyelograms were normal. Cystogram was repeated and showed more marked distortion and elevation of the bladder floor (Fig. 2).

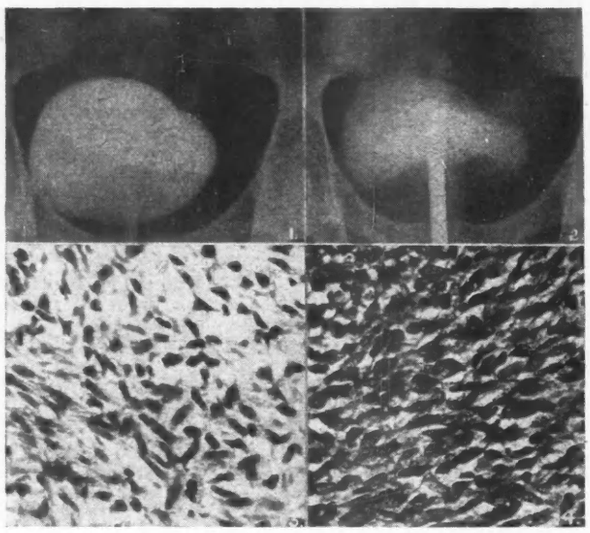

Fig. 1. (Case 1).—Cystogram taken October 30.

Fig. 2. (Case 1).—Cystogram taken November 3. Note further intrusion of the growth.

Fig. 3. (Case 1).—Biopsy specimen obtained at operation. x 400.

Fig. 4. (Case 2).—Section of prostate obtained at necropsy. Note similarity to section of case 1. x 400.

Diagnosis of malignancy of the prostate was made, probably sarcoma. Patient was given a series of deep x-ray treatments with only slight improvement. The prostate per rectum seemed to shrink a little, but then started to increase in size again.

November 24; cystostomy under general anæsthesia. A large mass was found projecting into the bladder anteriorly and from the floor on the left. The mass was larger than a regulation baseball. A portion of the anterior mass was enucleated, and 10 radium needles of 2 mgm. each were inserted into the mass. The needles were removed four days later.

The pathologist reported round and spindle cell sarcoma of the prostate (Fig. 3). The patient continued to have severe pains in the left leg, thigh, and sacro-iliac region. This was assumed to be due to pressure on, or involvement of the pelvic sympathetic nerve fibres. This view was supported by the change in skin thermal readings. On December 11, another series of x-ray treatments was started with no improvement in the patient's condition; and on December 23, the diary note stated—"Patient is going downhill, complains of aches and pains throughout body. Sedation is giving only slight relief."

By January 9, the prostate per rectum had increased in size. A right pleural effusion was found at this time. It was felt that the latter was probably due to pulmonary and pleural metastases.

The patient expired a week later, less than 3 months from date of admission. No autopsy was performed.

CASE 2

C.M., a 17-year old white male was admitted to the Orthopædic Service of the Royal Victoria Hospital on January 12, 1946, with the following history.

Four weeks prior to admission he complained of a dull ache in the left thigh which was aggravated by exercise and disappeared with rest. This pain left him after a few days, and he was well and up and about. One week later he went skiing, and fell several times. The following day the pain returned in the left thigh, and for the first time the left hip region was painful. About this time he noticed that he was having some difficulty in initiating the urinary stream, and this was accompanied by some pain when voiding. The severity of these symptoms was increasing daily. Patient was seen in the orthopædic out-patient department, and was admitted to the service for investigation.

Past history.—Patient had been perfectly well prior to the present illness. He noticed that since the onset of the above symptoms he was voiding more often, and in smaller quantities. Micturition was painful and difficult, and he occasionally had to get up during the night to void. No history of hæmaturia at any time. He denied exposure and venereal disease. Patient had been constipated during the past few weeks. The family history was non-contributory.

On physical examination he was found to be a pale, white male who complained constantly of pain in the left thigh. Temperature was 99°F. He lay in bed with his left thigh flexed, and any attempt to move the thigh was very painful. No other abnormality could be found in the hip, knee, or thigh. Chest was clear; blood pressure 120/68. There was no costo-lumbar tenderness. The bladder was distended above the symphysis pubis. The foreskin retracted easily, and there were no penile scars. The urethral meatus was clean, and there was no discharge present. Scrotum and contents appeared normal, the vasa were not thickened. The perineum appeared fuller han normal, and was tender on pressure. Rectal examination showed one thrombosed external hæmorrhoid. The prostate, particularly the left lobe was enlarged, boggy, and acutely tender.

The patient was unable to void, and an F. 14 soft rubber catheter was passed with some difficulty, and a large amount of urine obtained. Patient was then seen by the urological department and a diagnosis of abscess of the prostate was entertained.

Urinalysis showed a faint trace of albumen, occasional pus cell. Urine culture was taken, and later reported to contain diphtheroids, and lactobacilli. Phenolsulphonphthalein excretion was 55% in 2 hours. Leucocyte count was 10,600 per c.mm., blood chemistry was within normal limits. The blood Wassermann reaction was negative. Penicillin therapy was started immediately.

Patient was unable to void the following day, and was again catheterized. The catheter was retained in position. Fever continued, and the prostate seemed to get larger and more fluctuant.

On January 16, patient was operated on under spinal anæsthesia, and a perineal section was done. When the prostatic "abscess" was incised only broken down prostatic material was found and evacuated. The wound was packed, and a perineal catheter was inserted into the bladder, and sutured in position.

The catheter was removed on the third day, but the patient was unable to void, and the catheter was re-inserted. The perineal wound failed to heal, and bled repeatedly. Urine continued to dribble from the perineum, and he was never able to void per urethram. The prostate per rectum continued to increase in size. The perineal wound started to bulge, and bled more frequently and more profusely. The fever persisted, and the patient was obviously worse than when he was admitted. It seemed evident at this time that one was dealing with a malignancy of the prostate, probably a sarcoma.

On February 1, suprapubic cystostomy was performed for bladder drainage, and a biopsy of the prostate was taken. At operation the gland was greatly enlarged,

particularly on the left. It had lost its line of demarcation. The patient's condition deteriorated. He lost weight, and became paler in spite of repeated transfusions. He complained of aches and pains in the thighs, chest, and more or less throughout his body. He gradually became cachectic and passed into a semi-comatose state, and expired on February 15, approximately five weeks after admission.

Necropsy was performed shortly after death with the following findings: (1) sarcoma of the prostate—round and spindle cell type (Fig. 4); (2) metastases to the penis, bladder, pelvic bones, sacral plexus, rectum, vertebræ, para-aortic, mediastinal, and bronchial lymph nodes, lungs and pleuræ; (3) bilateral bronchopneumonia.

SUMMARY

1. Sarcoma of the prostate is a comparatively rare condition, and is very highly malignant; The symptoms are those of bladder neck obstruction; diagnosis is made too late; treatment is palliative; prognosis is very poor.

2. We have presented two cases of sarcoma of the prostate whose early symptom, namely pain, was due to early involvement of the pelvic sympathetic fibres. Both cases presented similar pictures and ran similar courses.

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AIR EMBOLISM DURING LABOUR

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Although many cases of air embolism have been reported as a complication of intravenous resuscitation therapy, artificial pneumothorax, injection of fluid into the uterine cavity with the purpose of producing abortion (Deadman), tubal insufflation, and during the puerperium, few have been reported as a complication of labour. The purpose of this report is to record such a case.

In 1667 Ride noticed that the introduction of air in large quantities into the veins of animals resulted in death. According to Hamilton and Rothstein, the first case of air embolism was reported by Beauchesne in 1818, since which time many cases have been reported. Air embolism associated with childbirth was reported as early as 1857 by May.

In a review of the literature there seems to be some difference of opinion as to the amount of air injected into the blood stream which is required to produce a fatality. According to Coles, Richardson and Hall, 480 c.c. of air is the minimum lethal dose. Dible *et al.* claim that considerably more than 100 c.c. is required to produce death; while Simpson states that the tolerance of the patient to air in the blood stream depends upon his general condition and that as little as 10 to 15 c.c. may be fatal. Moore and Braselton say, "In considering the dangers attending the entrance of air into the circulation one must distinguish between the systemic and pulmonary veins". Van Allen, Hrdina and Clarke proved this by experiments upon dogs. When air was injected into the pulmonary vein it took only 1.5 c.c. per kg. of body weight to kill the animal, while one dog withstood 76 c.c. per kg. when injected into the jugular vein.

There still appears to be some doubt as to the exact cause of death in pulmonary air embolism. According to Forbes death is due to one of the following causes: (*a*) interference with the expulsion of blood from the right ventricle (because of the compressibility of the froth); or (*b*) the froth may plug the pulmonary artery; or (*c*) the arterioles of the lung may become blocked with air bubbles. If the air enters the systemic circulation directly or passes from the lung capillaries to the veins when sufficient absorption has occurred to reduce the size of the air bubble to pass through the tiny vessels, death is due to blockage of the coronary or cerebral vessels.

The symptoms most commonly described are sudden onset, collapse, deep respirations, thready rapid pulse, restlessness, and chest discomfort. Osborn and Dawson state that if the case is fatal in one to two minutes and associated with fright, pallor is present, while if death is delayed, cyanosis is found. These authors also claim that convulsions are a rare symptom of air embolism.

So far as treatment is concerned it has been demonstrated by Fine and Fischmann that at least in rabbits the serious effects of air embolism that are not immediately fatal are prevented or rapidly alleviated by prompt administration of oxygen inhalation. It has been suggested by Behnke *et al.* that air embolism be treated by subjecting cases to oxygen at high atmospheric pressure and then gradual decompression.

Mrs. H.G.P., white, aged 32. This woman, whose last menstrual period was September 23, 1945, began her antenatal visits on December 8, when she was two and one-half months pregnant. At this time she stated that

she had had no unusual symptoms thus far. The family history was essentially negative with the exception that her mother had died of childbirth at the age of 32. The patient had one previous pregnancy which was normal in every respect. There were no past illnesses of any significance. Physical examination was negative. Blood pressure 128/78; Hgb. 78%; urine negative; weight 119 lb.

The patient faithfully reported for her monthly antenatal visits and on her visit of May 10, 1946, approximately her 8th month of pregnancy, considerable œdema of the feet, ankles and legs was noted. Her weight was 147 lb. (a rise of over 12 lb. in one month), blood pressure 162/94, and the urine contained a heavy trace of albumin. She was sent home to bed and advised to take a salt-free, high protein diet. Two weeks later her weight had risen to 153 lb., blood pressure 152/100, and the urine still contained a heavy trace of albumin. At this point she was admitted to the Kingston General Hospital. While in hospital she was put on a high protein, low salt diet, with a daily check on her weight, blood pressure, urine, and intake and output of fluids. During the ten days she spent in hospital her blood pressure fell to 122/82. She lost 14 lb. in weight but her urine still contained a heavy trace of albumin. She was discharged from hospital at this point and during the next two weeks a close check was kept on her and although her weight did not increase, her blood pressure did, while the urine remained unchanged.

She was again admitted to hospital, this time for the purpose of inducing premature labour. In spite of stripping the membranes on June 17, and of inserting a Voorhees' hydrostatic bag on June 18, labour failed to begin. The bag was removed on June 22 and because her condition had improved it was decided to let her go into labour of her own accord and in the meantime keep her in hospital under close observation.

On June 27 labour began at 6 p.m. and by 8 p.m. the pains were fairly strong, regular, and two minutes apart. At this time a temperature of 101° F. was recorded but aside from this nothing unusual was noted. At 10 p.m. the patient suffered a chill and shortly after 11 p.m. she vomited reddish-brown material which was thought to contain blood. At midnight she went into shock, became very restless and was cyanosed At this time the pulse was 150 and the blood pressure below 80 mm. Hg. Because the patient was losing considerable blood *per vaginam* we treated the shock with a blood transfusion in one arm and 10% glucose in distilled water in the other. At this time the fetal heart was heard running at 120 beats per minute. Oxygen inhalation was administered. In spite of the blood and oxygen the patient steadily went downhill. At 1 a.m. a stillborn baby was delivered spontaneously and at 1.30 a.m. the patient expired.

Summary of pathological findings.—An autopsy was performed about two hours after death. The first evidence of the cause of death came when the vessels of the breast were cut, at which time air bubbles could be seen escaping with the blood. When the heart was compressed and the right ventricle opened, air bubbles rushed out.

On opening the chest both lungs were found collapsed.

The liver was greatly enlarged and dark red in colour. It had the gross appearance of a diffuse, hæmorrhagic condition. On section the liver lobules stood out prominently and a few small yellowish areas could be seen. The wall of the gall bladder was markedly œdematous.

The stomach contained about 500 c.c. of blood-stained fluid and the gastric mucosa was hæmorrhagic.

Microscopic sections:—

Liver (Fig. 1).—The lobules stand out due to peripheral areas of hæmorrhage. In some of the areas of hæmorrhage, the liver cells have undergone necrosis. The intralobular sinusoids are markedly dilated and filled with blood. The liver cells in the central portion of the lobules show no appreciable pathological change. Stains for fat show a minimal amount of fine droplets distributed throughout the lobules.

Kidney (Fig. 2).—The glomeruli show catarrh of the endothelium in Bowman's capsule. Some capsules are dilated. Circumscribed vesicle-like spaces are occasionally present in the capillaries of the glomerular tuft which may be air bubbles. The tubules show changes from cloudy swelling to necrosis. In a few, the endothelium is separated, the cytoplasm contains fine granules and the nucleus is pale. In many, however, the protoplasm has been shed almost completely and the nuclei

Fig. 1

Fig. 2

are lost or are undergoing degenerative processes. The lumina contain cellular, granular, and hyaline casts. Stains for fat show a minimal amount in some of the convoluted tubules. The vessels appear normal and the stroma shows hyaline change.

Conclusion.—Death was probably due to air embolism. There is also gross evidence of toxic changes in the liver and kidneys.

DISCUSSION

In this case of air embolism during labour no other mode of entry for the air seems plausible except through the uterine sinuses. It is felt that the probable mechanism was, that following premature separation of the edge of the placenta, the air was pumped into the sinuses by each uterine contraction. A case of air embolism has been reported in a woman who sucked air into the open uterine sinuses when she adopted the knee-chest position following delivery. It is unlikely that such a mechanism took place here. One might say the air could have gained entrance to the circulatory system through the intravenous resuscitation measures. This is improbable because intravenous therapy was started after the patient was suffering from cyanosis and collapse. There was no obvious break in our usual method of administration.

As to how the air reached the systemic circulation, only one explanation seemed feasible to us and that was that the air bubbles became so reduced in size from absorption that they were able to pass through to the left side of the heart.

One could not find an adequate explanation for the hæmorrhagic gastric mucosa and the

bloody vomitus but it could have been the result of multiple infarcts in the stomach wall.

We also could not account for the collapse of both lungs, but again, this may have been the result of massive blockage of the vessels of the lungs.

The vaginal bleeding, noted during labour, possibly was due to low implantation of the placenta. This area of separation of the uterus from the placenta was probably the site of entry for the air.

It was interesting to note that, in spite of the apparent improvement of the toxæmia clinically, at autopsy this patient proved to be very toxic.

Just what part the introduction of the hydrostatic bag played in the production of the air embolism is problematical. However it was noted that most reported cases of air embolism associated with labour have usually been preceded by operative interference.

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A CASE OF PENTOSURIA

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Pentosuria is the condition in which an unusual reducing substance, one of the pentose sugars, is constantly excreted in the urine and gives a positive reaction on testing with Benedict's solution. It has been considered quite rare and only about two hundred cases have been reported in the literature but it is likely that many more cases will be found if the condition is suspected and the appropriate tests made.

It is obviously important to the patient from many points of view that he should not be given a diagnosis of diabetes mellitus if he has instead a condition which will be present all through his life without affecting his health, and one for which he should have no dietary restriction and no insulin. The proper diagnosis will also make a great difference in his rating for insurance purposes as the person with pentosuria should be considered normal as far as his ability to utilize sugar is concerned.

Most cases have been discovered by the finding on routine examination of a positive sugar reaction at all times in the urine, with a normal blood sugar and a normal glucose tolerance test; there are no diabetic symptoms and the urinary sugar is never large in amount. Most reported cases have been present in Jews, and predominantly in males, but the latter finding may be due to the greater number of males who have had life insurance examinations.

In the case to be reported here, sugar was found on insurance examination in 1927 and again later that year when he was admitted to hospital for an operation. In 1929 he came to my office to be treated for the supposed diabetes mellitus. I discovered that this was a case of essential pentosuria and along with Dr. Walter Campbell gave a preliminary report to the Section of Pathology of the Academy of Medicine, Toronto, on March 25, 1930. After that time the case was investigated more fully and the sugar was identified as d-xyloketose.

J.F., born in 1906, is a Polish Jew. He was examined on August 6, 1929. His only complaint was of constipation, for which he used mineral oil; as he was going to be married he wanted a general examination, with particular reference to the sugar that had been found in the urine two years before. There was nothing of note in the functional inquiry. In his past history the only point of interest was the operation which had been done on August 26, 1927. From the hospital records it was found that he had come in complaining of abdominal pain which had been increasing for a week; on admission it was very severe and crampy over the whole abdomen. The urine sugar was reported as two plus with no acetone and the white blood count was 20,800. Before operation he was given 10 grams of sugar and 10 units of insulin without a blood sugar estimation. At operation the only abnormal finding was a large boggy rectum filled with fæces; the abdomen was closed and he was given an enema. Three days later the blood sugar was recorded as 70 mgm. %.

Physical examination showed him to be a slight, poorly developed young man weighing 98 pounds. Blood pressure was 122/76, pulse 76 and regular; tonsils large but not infected; heart, lungs and abdomen were normal; rectal examination normal. The urine showed a positive reaction for sugar and was otherwise normal. The blood Wassermann was negative.

On August 11, 1929 the urine, fasting, showed sugar two plus and the blood sugar was 110 mgm. %. In my notes there is a question mark after this blood sugar report as it did not seem to fit in with the urine examination. On August 16 a glucose tolerance test was done with 100 grams of glucose and the following are the results:

TABLE I.

	Blood	*Urine*
	%	
Fasting	0.100	++
½ hour	0.127	++
1 hour	0.099	++
2 hours	0.092	+
3 hours	0.072	+

Following this test my original note is that "this is a case of renal glycosuria". If the investigation had stopped at that point he could have been told quite correctly that he did not have diabetes mellitus and that he should not restrict his diet.

The next point investigated was the fermentation with yeast. The sugar in this case did not ferment, while the control with glucose did ferment, with CO_2 production. Then the urine was tested with phenylhydrazine and an osazone formed which was in the typical shape of fine needles. The first attempt to determine the melting point of the crystals was not satisfactory as it gave a figure of 150° C., probably on account of impurities, but later with a larger amount of urine the osazone crystals were further purified and found to melt at 158° C.; therefore the sugar was d-xyloketose.

At the present time, January, 1947, this patient is in good health and still continues to excrete pentose in the urine. The final diagnosis is essential pentosuria.

COMMENT

In 1892 Salkowski and Jastrowitz[1] reported the first case of pentosuria. In 1900 Neuberg[2] found a pentose which was racemic arabinose and which formed an osazone with phenylhydrazine. Similar cases were described by Aron[3] in 1913 and Cammidge and Howard[4] in 1920. In these cases arabinose was described as the sugar present. In 1914 Levene and LaForge[5] found a dextro-rotatory pentose which they proved to be xyloketose; it formed an osazone with a melting point of 160° C. which when mixed with l-xylosozone formed a new compound, dl-xylosazone, which melted at 210° C. Other authors have proved the existence of xyloketose and in most of the cases reported to date it has been the sugar present. Garrod[6] in 1923 gave an excellent review of the literature and collected more than 50 cases of pentosuria. He included this condition among the inborn errors of metabolism.

In the earlier years it soon became recognized that there were two types of pentosuria, an alimentary and an essential pentosuria. Von Jaksch[7] proved that when unfermented fruit juices containing arabinose, such as cider, were taken in large quantities by certain individuals the urine during the next twenty-four hours frequently contained the pentose, arabinose. However in essential pentosuria the excretion of the pentose was not related to the composition of the diet and the disorder occurred almost entirely in the Jewish race.

Diagnosis and differential diagnosis. — The conditions with which pentosuria is most commonly confused are mild diabetes mellitus and renal diabetes. In a mild case of diabetes mellitus the urine is often free of sugar after fasting overnight but in pentosuria and renal diabetes sugar is present at that time. A useful test for pentose is described by Enklewitz and Lasker.[8] It is performed by adding 1 c.c. of urine to 5 c.c. of Benedict's solution and leaving it at room temperature for several hours. A positive test is not to be confused with a pseudo or phosphate reaction; the phosphate precipitate is white or gray in colour whereas in cases where the test is positive the precipitate is golden yellow and often forms a layer or rim above the phosphate precipitate after the tube has been allowed to stand for some time. With the exception of levulose, other sugars (glucose, maltose, lactose, xylose, arabinose and glycuronic acid) in similar weak concentrations (under 1%) do not reduce in the cold.

The following table summarizes the useful tests:

TABLE II.

	Pentosuria	*Renal diabetes*	*Diabetes mellitus*
Reducing bodies in urine:			
(*a*) fasting	+	+	0
(*b*) 2 hours p.c.	+	+	+++
Fermentation of urine.	Negative	Positive	Positive
Bial test	Positive	Negative	Negative
Sugar tolerance	Normal	Normal	Diabetic
Osazone melting point.	160° C.	204° C.	204° C.
Benedict's solution, (cold)	Positive	Negative	Negative

Symptoms.—Most authors consider that there are no symptoms that can be attributed to the pentosuria. An exception to this is Margolis[9] who found that 27% of his collected cases suffered from headache and that 77% were psychoneurotic. In regard to this latter point, Garrod[6] states that race and racial temperament play an important part and that the diagnosis of diabetes, commonly made, may contribute to the result.

SUMMARY

1. Essential pentosuria is a harmless error of metabolism which is frequently confused with diabetes mellitus.

2. Simple methods of testing for this condition are described.

3. A case is reported in which the presence of this sugar in the urine has been known for twenty years without affecting the patient's health.

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A CASE OF ACTINOMYCOSIS TREATED WITH STREPTOMYCIN

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I have just completed the successful treatment of a case of actinomycosis bovis with streptomycin, and thought that it may be worthy of record.

The patient was a male, aged 61, living in the town of Banff, but had been away on a month's holidays previous to his admission to hospital.

The history was, that seven days previous to my visit he had had a carious molar tooth extracted from his lower jaw. Two days after extraction he noticed a hard, rock-like swelling in the submandibular region. This swelling increased in size, until when I saw him, he was experiencing respiratory embarrassment and was unable to swallow.

The submandibular region was markedly swollen and extremely hard, with no sign of fluctuant or soft areas. There were no nodes palpable, either in the supraclavicular region or anterior to the sterno-mastoid muscle. The temperature was 100°, pulse 98 and there was a moderate degree of cyanosis.

He was immediately transferred to the hospital, placed in Fowler's position, and started on intravenous fluids, together with sulfadiazine gr. xv (crushed in solution) q.4h. and penicillin 200,000 units q.3h. intramuscularly.

The following morning the mass had progressed further posteriorly; patient was unable to swallow the sulfadiazine tablets (even when crushed). Respiratory embarrassment was marked to such an extent that we were prepared to perform a tracheotomy.

We obtained four small particles, having the appearance of sulphur granules, from the socket of the tooth. The technician's report on a crushed granule was that it showed thread-like branching filaments with formation of a ray fungus.

The patient was at this time in a critical condition, and the respiratory embarrassment and inability to swallow were becoming progressively worse in spite of treatment.

Streptomycin was obtained the following day. KI treatment and all other chemotherapeutic agents were discontinued and the new antibiotic streptomycin was given intramuscularly 250,000 units in 2½ c.c. of sterile water q.3h.

At the time treatment was commenced the clinical picture was that of a very sick patient, in that respirations were laboured and short, and he was unable to swallow even fluids without coughing.

Measurements of the mass were taken in a circling line including base of occiput ½ inch below the lobe of the ear, and one inch below centre of mandible across summit of swelling. Under treatment with streptomycin these showed a gradual reduction from a maximum of 20″ on November 20, to 18″ (normal measurement) on November 26. Streptomycin was given for 5 days, in the dosage mentioned. At the end of that time the condition had completely cleared up and the patient was discharged cured.

The following is a table of change in laboratory findings during the five-day treatment with streptomycin.

TABLE I.

Date	*Sedimentation rate*	*Pulse*	*Temperature*	*White blood cells*	*Polymorphonuclears*
Nov. 21..	47 mm.	90	99.4	13,450	80%
Nov. 22..	40 mm.	76	Normal	11,180	76%
Nov. 23..	30 mm.	76	"	8,500	75%
Nov. 24..	22 mm.	74	"	7,700	91%
Nov. 25..	18 mm.	76	"	7,000	90%

I have been unable to find the record of any case of actinomycosis treated with streptomycin. Potassium iodide, sulfadiazine, and penicillin were the other forms of therapy used in this case, without any effect on the fulminating course of the disease. When streptomycin therapy was started and all other antibiotics were discontinued the condition immediately subsided. We must therefore conclude that the streptomycin was responsible for the alleviation of symptoms in this one case.

I would like to extend my appreciation to Sister Helen Joseph, the Laboratory technician, and to Miss Benoit, R.N., both of Banff Mineral Springs Hospital for their compiling of case history and laboratory data.

SPECIAL ARTICLE

THE "FOLIC ACID" STORY

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In organic chemistry, a compound is defined in terms of its physicochemical properties, such as composition and melting-point and crystalline form, and these cannot be determined until the substance has been isolated in a pure state; in biochemistry, however, it is often necessary to confer names upon substances which have not been isolated and which are known only through their biological or pharmacological properties. Thus all the vitamins (and the hormones) were first defined in terms of their behaviour in living systems; though many have since been isolated and re-defined in chemical terms. The two kinds of definition may not be congruent: in some cases, it may be found that two or more chemically-different substances have the same biological properties; in other cases, that the biological reaction requires the participation of several unrelated substances; in others again, that a single substance underlies various biological phenomena separately studied and not suspected of possessing a common basis. All these are causes of confusion in nomenclature, and all may be exemplified in the story of folic acid and its relatives. The difficulty of unravelling their story is increased by the fact that a number of the papers published in this commercially-significant field have displayed an unedifying desire to claim priority in discovery but to divulge as little information as possible.[1] Since these substances, though among the latest additions to the vitamin B complex, have already proved more important in practical medicine than many long-known factors, it may be useful to survey the group without attempting an exhaustive review.

The name *folic acid* was given by Mitchell, Snell and Williams[2] to a growth-factor for the micro-organism *Streptococcus fæcalis* R (originally but erroneously regarded as a strain of *Streptococcus lactis*[3]); it was found in spinach and concentrated to a high degree of purity. It has not, however, been crystallized, and as only 1.2 milligrams of the purest form were obtained the definition of the physicochemical properties is very incomplete. It is, therefore, impossible at present either to affirm or to deny the identity of this substance with substances of similar biological properties found by the same workers in other leafy plants (hence the name folic acid), or by other workers in liver and in other fields. The name folic acid should, therefore, strictly speaking, be restricted to purified preparations from spinach, and will be so used in this review, except when placed between inverted commas; but it has, in fact, been loosely used for any substance which in the defined media stimulates the growth of *Str. fæcalis* R. True folic acid also, under suitable conditions, stimulates the growth of the *Lactobacillus casei* ϵ of Freudenreich, and many workers have preferred to use this test; but, as will be seen, the two tests are not interchangeable.

A factor for *Lb. casei* had, indeed, been discovered in yeast and in liver[4] before the existence of folic acid in spinach was reported. It was concentrated as a "norite eluate", that is to say, it could be adsorbed on norite charcoal and removed therefrom by ammoniacal alcohol, and it was found to be required by many micro-organisms,[5] including *Str. fæcalis* R. The substance from liver was further concentrated and crystallized by Pfiffner and his collaborators,[6] and its chemical structure was worked out and confirmed by synthesis.[7] It is a yellow compound of the hitherto-unknown "pteroic acid" with the familiar amino-acid glutamic acid and though the product is often called "synthetic folic acid" it may be more accurately designated "pteroyl-glutamic acid". If it is true that the best preparation from spinach (which is 137,000 times as active as the crude liver fraction used as a standard) is virtually pure, then the activity of folic acid for both *Str. fæcalis* and *Lb. casei* is the same as that of pteroyl-glutamic acid (synthetic or from liver),[8] and the substances may well be chemically identical; but there is no definite proof.

Meanwhile Hutchings and others[9] obtained crystals, from a source later and vaguely described as a "fermentation product", which were certainly different, and have since been shown[7] to contain two additional molecules of glutamic acid; this material may thus be called "pteroyl-triglutamic acid". The activity of this for *Lb. casei* is 85% of that of the liver factor, a difference explained by the greater size of the molecule, but the activity towards *Str. fæcalis* is only about 5%, and it is permissible to suppose that the latter organism has difficulty in spitting off the extra glutamic acid. An enzyme has been found in rat liver and chick pancreas which apparently accomplishes this splitting, thus increasing the activity of Hutchings's substance towards *Str. fæcalis* twenty-fold. The actual concentrations required for half-maximal growth under prescribed conditions are: for *Lb. casei,* 0.000055 and 0.000061 micrograms per c.c. medium, for pteroyl-glutamic and pteroyl-triglutamic respectively; for *Str. fæcalis,* 0.00025 and 0.0042 respectively. Still another compound which seems to have intermediate properties had been crystallized from yeast by Stokstad;[10] its chemical nature is unknown, but it is reported as having the same activity towards *Lb. casei* as pteroyl-glutamic, but only half of the latter's activity towards

Str. fæcalis; a suitable mixture of pteroyl-glutamic and pteroyl-triglutamic would have such properties, but presumably would not behave like a single substance in crystallization.

Keresztesy, Rickes and Stokes[11] reported, very briefly, the "isolation" of a substance highly active for *Str. fæcalis* but almost inactive for *Lb. casei*; this adds to the complexity, since a mixture of Keresztesy's factor with Hutchings's would, like folic acid and pteroyl-glutamic acid, be active for both organisms. It is possible that Keresztesy's substance, whose chemical properties have not been described, is identical with glutamic-free pteroic acid, which has been prepared synthetically and has qualitatively similar biological properties;[7] if so, it may be supposed that *Streptococcus* is able and *Lactobacillus* unable to attach the glutamic acid. Something of the sort evidently does occur; for when *Str. fæcalis* is grown in presence of Keresztesy's factor, the medium gradually becomes able to support the growth of *Lb. casei.*

Some years earlier, Hogan and Parrott[12] described a factor present in liver which was required to permit full growth and to prevent a macrocytic anæmia in chicks fed on purified rations; they designated this "vitamin Bc" (c for chick), and it is probably identical with an earlier chick "Factor U".[13] As the purification of pteroyl-glutamic acid proceeded, it became increasingly evident that it was related to Bc, and it was as Bc that Pfiffner[6] referred to his crystalline preparation. In fact, both pteroyl-glutamic (synthetic or natural) and pteroyl-triglutamic acids are effective in preventing chick anæmia, in doses around 2.5 micrograms per gram of ration. In yeast and many foods, however, there may be found a substance very effective in the chick, but inactive towards both *Lb. casei* and *Str. fæcalis.* This material has been crystallized,[6] and on incubation with crude enzyme preparations obtained from rat liver, hog kidney, etc., it breaks down to yield pteroyl-glutamic acid, identified both chemically and biologically. The material is evidently, therefore, a "conjugate" of pteroyl-glutamic acid ("Bc") with unknown substances, and higher animals such as the chick can, unlike the test micro-organisms, destroy it and obtain pteroyl-glutamic acid from it; it would be interesting to know whether this breakdown occurs in the alimentary canal, but the conjugate does not seem to have been administered parenterally. The nature of the conjugate is unknown; it is not a protein, but the "Bc-conjugase" enzyme is very probably identical with that which breaks pteroyl-triglutamic to pteroyl-glutamic acid and thus evidently attacks peptide-type linkages. The possibility that the conjugate contains other nutritionally-important substances in addition to pteroyl-glutamic acid should not be overlooked.

Other workers have described chick factors "B_{10}" for feathering and "B_{11}" for growth:[14] these may be free from activity for *Lb. casei,* but their separability from the above-mentioned conjugate does not seem to be established. Pteroyl-glutamic acid has an influence on feathering.[15]

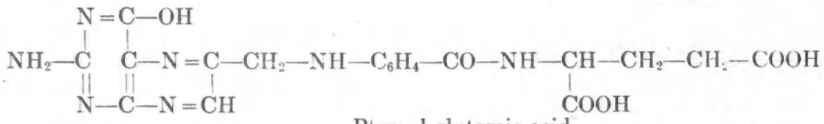
On certain unbalanced diets, monkeys develop hyperchromic anæmia with megaloblastic hyperplasia of the marrow, and severe leukopenia;[16] Day and his group[17] postulated a vitamin "M" (for monkey) found in brewer's yeast and elsewhere. The deficient animals develop diarrhœa, ascribed[18] to a lowering of their usually high resistance to bacillary dysentery. The deficiency can be relieved by the administration of pteroyl-glutamic acid, whether free or conjugated, and the nature of vitamin M is therefore, at least in part, elucidated. The guinea-pig also requires vitamins of the folic-acid family,[19] but in the rat it appears that such substances are normally synthesized in adequate amounts by intestinal bacteria. Oral administration of succinyl-sulfathiazole alters the cæcal flora and makes it possible to demonstrate the development of granulocytopenia and anæmia responsive to "folic acid".[20] Such factors may also be required by the fruit-fly *Drosophila*[21] and the mosquito *Ædes.*[22]

Xanthopterin is the name now given to an orange-yellow pigment found in the wings of butterflies (*Pieridæ*) by Hopkins[23] over fifty years ago. It was encountered much more recently in the yellow stripes of wasps, in urine, and in liver extracts; its structure has been established by synthesis. It has been found efficacious in preventing the troublesome anæmia of hatchery-reared trout fry;[24] folic acid itself seems to be rather less effective.[2] Xanthopterin is said to be not inactive in the anæmia of rats fed on goat's milk,[25] and in "M-deficient" monkeys. Its absorption spectrum is similar to that of folic and pteroyl-glutamic acids,[2, 5] though less intense, and it is claimed that the addition of xanthopterin increases the yield of *Lb. casei* activity when incubated with liver.[26] This may mean that xanthopterin partially replaces pteroyl-glutamic acid in metabolism, rather than that there is any interconversion. Xanthopterin does not seem to stimulate the growth of micro-organisms.

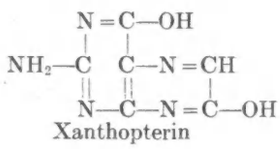
The chemist has long been familiar with *para*-amino-benzoic acid, which attracted biochemical attention when it was shown to protect certain micro-organisms against sulfanilamide. The two substances being chemically similar, Fildes[27] suggested that *para*-amino-benzoic was an essential growth-factor for these species (it inhibits *Rickettsia,* however[28]), and that sulfanilamide might be sufficiently similar to be drawn into the metabolic machinery, but sufficiently dissimilar to "gum up the works" and prevent growth. This theory may now stand in need of some modification, but in the meanwhile it has led to a vigorous and not unfruitful search for other bacteriostatic agents re-

sembling other growth-factors.[29] Attempts to show that *para*-amino-benzoic acid is a vitamin for higher animals have not been very convincing;[30] the observed effects could in general be interpreted as effects primarily upon the intestinal flora.[31] But our outlook on all this has changed with the demonstration[7] that pteroic acid is a compound of *para*-amino-benzoic acid with a molecule resembling xanthopterin. It is uncertain that *para*-amino-benzoic acid has any function in metabolism, mammalian or bacterial, other than that of contributing to "folic-acid" formation.

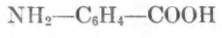
So far as clinical trials are concerned, only those conducted with relatively pure or synthetic pteroyl-glutamic ("folic") acid need be discussed. The animal experiments suggested its use in leukopenia, as for example after x-ray therapy, but the results have not been very encouraging.[32] On the other hand it has fully proved its value in certain types of anæmia, those in which the pro-erythroblasts give rise to megaloblasts rather than to normoblasts, and which are invariably macrocytic and hyperchromic.[33] With doses of 10 to 20 mgm. daily, orally or more often parenterally, striking results have been obtained in Addisonian pernicious anæmia,[34] in sprue either tropical[35] or non-tropical,[36] in nutritional macrocytic anæmias[37] and the macrocytic anæmias of pregnancy;[38] a reticulocyte response leads to a steady rise in hæmoglobin and erythrocyte-count. Perhaps the most dramatic cases are those with tropical sprue, where the response



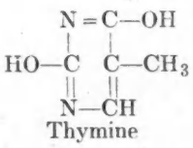
Pteroyl-glutamic acid



Xanthopterin



Aminobenzoic acid



Thymine

to ordinary liver extracts and dietary treatment may be very disappointing, and where "folic acid" may rapidly control the diarrhœa in addition to evoking reticulocytes.

The relationship between "folic acid" and the longer-known factors effective in pernicious anæmia remains obscure. The work of Castle[39] and others has led to the theory that there is in many foods an unidentified vitamin-like "extrinsic factor", which is acted on by an enzyme-like "intrinsic factor" (possibly an amino-polypeptidase[40]) present in normal gastric juice; the heat-stable product of this reaction is absorbed and stored in the liver, whence it may be recovered in concentrated but still impure form, and whence it is presumably distributed in health to control erythropoiesis. Thus megaloblastic anæmia might theoretically result from absence of "extrinsic factor" from the diet (tropical nutritional macrocytic anæmia), or of "intrinsic factor" from the gastric juice (pernicious anæmia), or from failure to absorb the product of the reaction (sprue), or from failure of the hæmopoietic organs to respond to that product (achrestic anæmia); the poor response of some cases of nutritional anæmia or sprue to liver-extract injections remains unexplained. How can pteroyl-glutamic acid be fitted into this story? It is not identical with "extrinsic factor" since it is active even when "intrinsic factor" is lacking; it certainly is not "intrinsic factor". Concentrated anti-anæmic liver extracts contain "folic acid" (measured by microbiological tests[41]), but not in amounts sufficient to explain their activity; indeed, the best liver extracts[42] seem to be more active, weight for weight, in pernicious anæmia than is pure pteroyl-glutamic acid. In a recent exhaustive review[43] it is suggested that the liver substance in some way mobilizes "folic acid" from the tissues, and that it is the latter that participates directly in erythropoiesis. Other equally speculative interpretations might be worked out; for example, that the true anti-anæmic substance is produced from pteroyl-glutamic acid with only moderate efficiency, perhaps in the liver, and that the "intrinsic factor" is a "Bc-conjugase" in whose absence pteroyl-glutamic acid (which occurs chiefly in conjugated form in foods) is available in quantities too small to keep the inefficient conversion going. The true answer may be simpler than now seems possible.

There is some evidence to suggest that "folic acid" serves to promote the synthesis of thymine, a pyrimidine base found in all known nucleoproteins. *Str. fæcalis* will grow in the absence of "folic acid" if large amounts of thymine are supplied, and in this case (unlike the case where pteroic acid is supplied) there is no formation of "folic acid" in the culture;[44] similar observations have been made with *Lb. casei*. Thymine, in doses up to 10 gm. daily, is effective in pernicious anæmia.[45] In all these cases pteroyl-glutamic acid is more than a thousand times as active as thymine, hence its rôle, if real, must be catalytic, and analogous to the rôle of copper in hæmoglobin formation.

SUMMARY

The more important substances described in this review may be listed in order of increasing complexity.

1. *Xanthopterin* is a yellow pigment related to the purines: in natural or synthetic form it prevents a type of anæmia in trout-fry[24] and perhaps to some extent in other animals, but seems not to be a growth-factor for micro-organisms.

2. *Pteroic acid* is a synthetic compound of a methyl-desoxy-xanthopterin with *para*-amino-benzoic acid; it promotes the growth of *Streptococcus fæcalis* R but not that of *Lactobacillus casei*,[7] and in this property at least it resembles a substance isolated by Keresztesy.[11] Both appear to be inactive in animals.

3. *Pteroyl-glutamic acid* has been isolated from liver[6] and prepared synthetically;[7] it is active for both *Str. fæcalis* and *Lb. casei;* in this it resembles *folic acid*,[2] concentrated from spinach, and the two may be identical.

4. An unidentified substance isolated from yeast resembles pteroyl-glutamic acid, but is only half as active for *Str. fæcalis*.[10]

5. *Pteroyl-triglutamic acid*, isolated from fermentation products,[9] resembles pteroyl-glutamic in its activity towards *Lb. casei*, but has little activity for *Str. fæcalis*.

6. A *conjugate* has been isolated from yeast and is present in many foods; it is devoid of microbiological activity, but on enzymatic breakdown it liberates pteroyl-glutamic acid. It is tempting to regard this conjugate as a pteroyl-polyglutamic acid, since (*a*) the "conjugase" enzyme may well be identical with that which converts pteroyl-triglutamic into pteroyl-glutamic, and (*b*) a peptide consisting of one molecule of *para*-amino-benzoic and thirteen of glutamic has been isolated from yeast.[46]

Pteroyl-glutamic acid, folic acid, pteroyl-triglutamic acid, and the "conjugate" are probably all effective in relieving macrocytic anæmia and leucopenia in (*a*) the chick showing deficiency of "vitamin Bc", (*b*) the monkey showing deficiency of "vitamin M", (*c*) the guinea-pig showing deficiency of "GPF-2", (*d*) the succinyl-sulfathiazole-treated rat on purified diets. There may also, however, be other factors involved in these deficiencies. Pteroyl-glutamic acid is effective in the treatment of pernicious anæmia, sprue, and other megaloblastic disorders of erythropoiesis;[43] it cannot be identified with the active principle of anti-anæmic liver extracts, and may play a catalytic part in the synthesis of thymine.

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CLINICAL and LABORATORY NOTES

TETRAETHYL AMMONIUM CHLORIDE: A NEW DRUG USEFUL IN THE FIELD OF PERIPHERAL VASCULAR DISEASES

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Montreal, Que.

In the past year the Ann Arbor Group have developed a new drug, tetraethyl ammonium chloride, which has the effect of temporary paralysis of the autonomic nervous system. This blockade occurs at the ganglionic synapses and affects both the parasympathetic and sympathetic components. As might therefore be expected, administration results in a generalized vasodilatation and increase in skin temperatures, usually a lowering of blood pressure which may be extensive in hypertension,

some increase in pulse rate, cessation of sweating, dryness of the mouth, cessation of intestinal peristalsis and atony of the bladder. The main field of usefulness to date is in the sympathetic paralysis produced, and the effect appears to be as good in the production of vasodilatation as are the accepted methods of sympathetic procaine block, local nerve block or general and spinal anæsthesia. Tetraethyl ammonium chloride is consequently chiefly used in the investigation and occasionally as a therapeutic procedure in the various functional and organic vascular states such as Raynaud's disease, Buerger's disease, arteriosclerosis obliterans, acrocyanosis, pernio, trench foot, thrombophlebitis, causalgic states including herpes zoster and the reflex sympathetic dystrophies.

Administration is by the intravenous route depending on the length of time the effect is desired, lasting up to one hour in the former and six hours in the latter. Because of marked postural hypotension caused when standing, the patient must be in horizontal position for the above periods of time. Dosage is 200 to 500 mgm. when given intravenously and 10 mgm. per kilogram of body weight intramuscularly. The drug is non-toxic and rapidly excreted and the only untoward effect is the occasional marked drop in blood pressure in hypertensives. This can however be readily counteracted by adrenalin.

Tetraethyl ammonium chloride is produced by Parke, Davis and Company in a 10% solution under the trade name of Etamon, but is not as yet on the general market.

REGULATIONS FOR THE USE OF SHORT-WAVE DIATHERMY EQUIPMENT

If you employ short-wave diathermy in your practice, the law on the suppression of radio interference is of vital importance to you. Briefly stated, you are required to suppress the radiation from short-wave diathermy machines effective January 1, 1948. Most therapeutic radio-frequency generators now in use, because of inherent frequency instability, will not be permitted to operate after January 1, 1948, without being adequately shielded. The Canadian Broadcasting Act, 1936, included a section for the control of radio interference, and regulations were subsequently made under this Section in February, 1941. Owing to the shortage of material during the war, it was considered impracticable to enforce these Regulations with regard to short-wave diathermy equipment. As material is now available, and the interference is becoming more and more critical, all interference of this type must be suppressed.

Radiation from electro-medical apparatus including tube-type diathermy and short-wave machines occurs in two ways: (*a*) into space in all directions and for great distances; and (*b*) along power transmission lines. This radiation of energy is causing serious interference to radio communication as the radiations are transmitted on frequencies allotted to radio aids to navigation, aviation communication and control systems, etc. It will readily be appreciated that interference of this type is far more serious than extraneous noises on your favourite radio program, as it is capable of producing hazards to life.

By agreement between the Department of Transport in Canada and the Federal Communications Commission in the United States, three radio frequencies have been allotted to non-communication radio frequency generators, which include electro-medical equipment, and manufacturers are now producing short-wave diathermy machines which maintain their allotted frequency within the limits proposed.

As the responsibility for suppressing the interference lies with the user of the apparatus, two courses of action appear to be open to doctors who employ electro-medical equipment. These consist of (*a*) replacing existing equipment with new frequency-controlled units; or (*b*) providing adequate shielding for existing equipment. Either of these alternatives will subject the user to considerable expense, in the first case for the purchase of new equipment, or in the latter instance in providing a completely shielded room, booth or cubicle, as well as a surge trap or filter for the power lines.

Full technical details of the requirements have been incorporated in the following memoranda issued by the Department of Transport, Radio Division: SII-13-25 dated December 11, 1941; SII-13-28 and SII-10-39 dated October 19, 1946.

Advice, testing and inspection services are available to users of electro-medical equipment by consulting the local representatives of the Radio Division of the Department of Transport listed below.

It is important that you prepare to comply with the regulations which will become effective in less than one year. Investigate the possibility of adapting your present equipment so that interference is actually suppressed and, if you are considering the purchase of new equipment, be sure that it complies with the new requirements.

The Controller of Radio, Department of Transport, Ottawa.

The District Superintendent of Radio, Department of Transport, 413 - 418 Belmont Building, Victoria, B.C.

The Supervising Radio Inspector, Department of Transport, 539 Public Building, Winnipeg, Man.

The Supervising Radio Inspector, Department of Transport, 566 Dominion Public Building, Toronto, Ont.

The Supervising Radio Inspector, Department of Transport, 404 Public Building, Calgary, Alta.

The Supervising Radio Inspector, Department of Transport, 400-401 Public Building, Regina, Sask.

The Supervising Radio Inspector, Department of Transport, 400 Youville Place, Montreal, Que.

The District Superintendent of Radio, Department of Transport, P.O. Box 217, Halifax, N.S.

A BLOOD SUGAR TEST*

Solomon Gold, M.D.

Montreal, Que.

The blood sugar test which will be described, is suggested mainly for its simplicity. It can be performed in any general practioner's office with materials usually available there. All that is needed is: 1 or 2% acetic acid, a hypodermic syringe, a long needle, standard test tubes (Pyrex test tubes, 5" x 5/8"), a spirit lamp and Benedict's solution.

TECHNIQUE

Five c.c. of blood is withdrawn in the usual manner. The needle is removed, and the blood is gently emptied into a dry, chemically clean test tube, and allowed to stand until sufficient serum is formed. One may hasten the process by centrifuging the blood as soon as coagulation sets in.

To 1 c.c. of blood serum or plasma, add ½ c.c. of 1% acetic acid. Boil well. Add 2 c.c. of Benedict's solution. Shake well by covering the opening of the tube with finger. Boil the solution well until the coagulum rises from the bottom, and allow to cool at room temperature, and note the colour.

Roughly speaking, blue denotes a low blood sugar; yellow, mustard or mustard orange, a high blood sugar; and green, a normal or slightly elevated blood sugar.

Thus it becomes apparent that the very low and the very high blood sugars can be easily diagnosed. The problem becomes less simple when one is dealing with a normal, or a slightly elevated blood sugar, since the colour here will be green. It becomes self-evident, that since green is made up of blue and yellow, a great range of values will be possible, depending on the relative proportion of the blue to the yellow. It becomes therefore necessary to break down the green into different gradations of tones.

It has been found that the density of yellow is directly proportional to the concentration of glucose in the blood. Accordingly, it is possible to grade the percentage of blood sugar in terms of colour. I have used the Ostwald Colour Standards† as a comparative guide and after testing many samples of blood have found that the amount of sugar present may be expressed by the shade of colour it produces. The following table shows the correspondence between the percentage of blood sugar and the colours of the Ostwald standards.

TABLE I.

Quantity of glucose mgm.%	*Corresponding shade of colour according to Ostwald grading*
40 - 50	ne, 18
60 - 70	ne, 19
80 - 100	ne, 20
110	ne, 21
120 - 130	ne, 22
140	ne, 22 - 23
150 - 160	ne, 23
180 - 200	ne, 23 - 24
200 - 250	pg, 24
300	ne, 2
Over 400	Mustard ochre

I have also compared the results obtained by the Folin Wu method of estimation, in a large series (over 200 samples) and give the results in the following table.

TABLE II.

A COMPARISON BETWEEN THE RESULTS OBTAINED BY THE FOLIN WU METHOD, (JEWISH GENERAL HOSPITAL AND ROYAL VICTORIA HOSPITAL), AND MINE [S.G.]

Date	*Case No.*	*Mgm. glucose per 100 c.c. of blood*	*Mgm. glucose per 100 c.c. of blood*
		J.G.H.	Mine
Dec. 18/46	56,004	242	200 plus
	56,794	127	110
	56,545	150	120
	56,699	196	200
Dec. 23	56,848	97	100
	56,864	120	130
	56,699	150	140
	56,798	197	200
Dec. 26	1,449	108	160
	5,684	167	180
	56,920	225	220
	54,545	360	300 - 400
Dec. 23. (12.00 noon P.C.)		R.V.H.	
	14,148	129	130
	17,736	40	60
	17,598	95	120
	17,039	55	70
	17,457	127	110
Dec. 26. (2.30 p.m. P.C.L.)	17,058	149	150
	17,457	156	160
	17,736	90	90
	17,598	168	160
	18,199	253	180

However, in the absence of a standardized colour chart, one may make use of ordinary colours. Thus:

Blue corresponds to less than 80 mgm. % of glucose.

Blue with a faint tinge of green (less yellow than olive green) to 100 mgm. %.

* Read before the Montreal Clinical Society, February 26, 1947.

† These are internationally accepted standards of colours. Those quoted above are taken from Series VIII, Plate 9 of the Ostwald Colour Standards. These Standards are obainable from Messrs. Winsor & Newton Ltd., 38 Rathbone Place, London, W.1., Eng., or from local art dealers.

Olive green to 120 to 140 mgm. %.
Chartreuse green to 150 to 180 mgm. %.
Yellow tinged green to 200 mgm. %.
Mustard ochre to 400 mgm. %.
Light orange to 500 mgm. %.

GENERAL OBSERVATIONS AND REMARKS

Some sera tend to deteriorate on standing too long at room temperature. To eliminate this possibility, it is advisable to test for glucose within 4 hours after taking the blood. Oxalated blood serum kept under refrigeration however, seems to be less affected by long standing.

TABLE III.
BLOOD SERUM (OXALATED) 36 HOURS OLD
(KEPT IN REFRIGERATOR)

Date	*Case No.*	*Mgm. glucose per 100 c.c. of blood*	*Mgm. glucose per 100 c.c. of blood*
		J.G.H.	Mine
Dec. 31/46	56,968	102	80 - 100
	56,493	118	140
	56,932	169	150
	56,545	168	170
	56,920	189	180 - 200

TABLE IV.
BLOOD SERUM (OXALATED) 96 HOURS OLD
(KEPT IN REFRIGERATOR)

Date	*Case No.*	*Mgm. glucose per 100 c.c. of blood*	*Mgm. glucose per 100 c.c. of blood*
		J.G.H.	Mine
Dec. 31/46	56,798	206	200
	56,939	120	140
	56,938	93	110
	56.934	118	80 - 100

One and two per cent acetic acid solution were tried. The 1% was found somewhat more sensitive. Four per cent acetic acid solution was found quite unsatisfactory, since even the moderately high blood sugars were found negative.

The following substitutions were made for the 1% acetic acid, and were found unsatisfactory for stated reasons. *Water*, plain and distilled, usually gave a greyish blue gel, with streaks of orange in the high sugar concentrations. *Hydrochloric acid* and *trichloracetic acid*, in various concentrations, gave a cloudy mixture, with a poor, inconsistent colour display.

Special care is to be taken to wash the syringe after using it for Benedict's solution, if the same syringe is to be used for drawing up the serum or the acetic acid. It was found that one drop of Benedict's solution added to the serum, acetic acid, or plasma-acetic-acid solution, before it had been boiled, gave a negative result, even in the case of a positive blood sugar.

Although it is preferable to have a clear serum, a small admixture of red blood cells, or hæmoglobn, will not affect appreciably the outcome of the test.

After the final boiling, the solution should be allowed to cool at room temperature, as cooling it under the cold water tap will spoil the test, and even the high blood sugars will give a negative result, due to the rapid cooling. The serum with the acetic acid should be boiled well until the whole solution is converted into a whitish frothy substance (it takes about one-half a minute on an alcohol lamp). Care is to be taken that it does not spill over.

The coagulum. — After the final boiling, a coagulated mass will be found floating in the solution. This coagulum can be left alone, or removed en masse.

Pouring off the hot solution into a cold test tube will diminish the positivity of the test, probably due to the more rapid cooling of the solution.

The colour reading is to be done in a good direct light, preferably natural or artificial day light. If a precipitate has formed, it is essential to shake the tube well, before reading the colour.

The precipitate.—In low sugars the precipitate is slate-grey, and remains so even after 24 hours' standing. In the presence of detectable glucose, the precipitate will, after standing for twelve hours or more, become yellow or orange, the quantity varying from a mere speck to a considerable deposit at the bottom of the test tube. Blood sugars below 100 mgm. % gave a persistent slate-grey, whilst those above 120, gave a yellow or orange, after long standing.

SUMMARY

A simple test for sugar in the blood is suggested which will aid in the diagnosis of a high and low blood sugar, and draw attention to doubtful cases, which should be subjected to further investigation.

The non-sugar reducing substances present in the serum were not taken into consideration since they are fairly constant and hence did not affect the colour differences appreciably.

The waning of tuberculosis, apparent in all countries with advanced civilization, has been less spectacular than the conquest of other diseases, but has meant a greater change in the well being of the population, and a greater rise in its average longevity, than the eradication of any other. Under way at least a century ago, it has continued with only occasional interruption to the present. The factors responsible have been lengthily debated, and the influence of specific anti-tuberculosis measures seriously questioned. In more recent years, however, there has been little argument against the claim that organized anti-tuberculosis campaigns have at least definitely accentuated an already favourable process. It is probably a fair statement that, if the anti-tuberculosis campaign is not yet responsible for the decline of tuberculosis, its organization is so powerful, and its principles so sound, that it must inevitably become so. —The Decline of Tuberculosis, E. R. Long, *Bull. Hist. Med.*, **8**: 819, 1940.

THE CANADIAN MEDICAL ASSOCIATION

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EDITORIAL

THE CAUSES OF SUDDEN DEATH

IT is well known that sudden death may occur in apparently healthy subjects, and also that in a certain proportion of these the cause of death is unknown. One of the latest studies on this problem is by Moritz and Zamcheck.* They have had the opportunity of reviewing the autopsy material at the U.S. Army Institute of Pathology for the period 1942-1946. In that time more than 40,000 protocols were received, and amongst these were reports of about 1,000 unexpected deaths, from disease, in previously healthy soldiers between 18 and 40 years of age. The source material was particularly instructive since the conditions of military life tended to produce closer surveillance of the subjects through their physical examinations and their ready access to hospital than would have been likely in civilian practice.

On general review it was thought at first that the body weight of those dying unexpectedly from disease was greater than that of the average soldier; actually the records stated this to be the case. But on careful analysis, the figures given could not be accepted. For example, a group of soldiers killed in motor or other accidents showed a greater frequency of overweight than the average soldier, which was not reasonable. The conclusion reached therefore was that there was a tendency for pathologists to overestimate the weight of dead bodies; or possibly that the average soldier was heavier than the average inductee.

Heart disease was accountable for the largest proportion of deaths, arteriosclerosis being the leading cause. In none of the cases in the group had the condition been suspected, and even in retrospect less than 25% had symptoms which might have been thought to be even suggestive. And yet in all instances severe arteriosclerosis of one or both coronary arteries was found.

Intracranial hæmorrhage provided the next largest group, and proved to be principally subarachnoid, arising from the rupture of a superficial aneurysm of the congenital or berry type. Many died during their first episode of bleeding, but others showed postmortem evidence of previous unrecognized bleeding.

In about one-third of cases of meningococcæmia death occurred within 24 hours after the onset of incapacitating symptoms. Since in a large proportion of cases the men were reported to have been below par or to have had a mild infection of the upper respiratory tract before fulminating symptoms developed, it is urged that such minor indispositions in men who are exposed to meningococcic infections should not be ignored. An unusual case of rapid death from meningitis is included, with well marked clinical evidence of the disease, but complete absence of laboratory evidence; the adrenals were grossly hæmorrhagic; the meninges showed no inflammatory change, although the blood and spinal fluid (postmortem) showed group 2A meningococcus. Miscellaneous causes included inflammatory, degenerative and neoplastic diseases of a wide variety, the largest sub-group probably being infections of the respiratory tract.

Perhaps the most interesting group however was that in which no cause at all for death could be found. There were at least 140 such cases which were very carefully investigated, without result. Apparently this obscurity of causation of sudden death will remain as a very difficult problem in pathology.

* Sudden and Unexpected Deaths of Young Soldiers: Diseases Responsible for Sudden Deaths During World War II, Alan R. Moritz, Boston, and Captain Norman Zamcheck, M.C., U.S. Army: *Arch. Path.*, **42**: 459, 1946.

THE COAL SHORTAGE ISSUE OF THE BRITISH MEDICAL JOURNAL

MEDICAL Journals have various ways of attaining fame; the quality of their contents—naturally the most impressive; their length of existence; conditions under which they are produced. The *British Medical Journal* has high qualifications in all these respects, but in the last named it has added to its striking war record by creating what are probably unique issues, in its numbers for Feb. 22 and March 1, 1947. These were in the

form of a 4-page stencil, the "printer" being the Secretary of the B.M.A., and of course was the result of the coal shortage and cutting off of power for printing.

This number should become a "collector's piece" if for no other reason than as a record of courageous resourcefulness and excellent editorial selection. There is in it a short, dispassionate (almost incredibly so) comment on what medicine owes to coal. But all the endless magic that is extracted from coal does not equal the fine spirit in which its deprivation has been endured. We should like to pay our tribute of respect to the Editor and staff of the *B.M.J.* for their struggle against such odds, adding sympathetic wishes for a happy and early issue out of all their afflictions.

EDITORIAL COMMENT

Electro-Medical Apparatus and Radio Interference

We publish in this issue regulations regarding the use of short-wave diathermy equipment. It must be generally recognized that this type of electrical apparatus causes radiations which interfere with radio reception. The extent of this interference varies, but at all times it is a direct source of danger through its effect on radio aids to navigation and control systems. For this reason it is imperative that electro-medical apparatus should be properly safeguarded so as to eliminate this interference. The Department of Transport, Radio Division, has issued regulations in connection with this safeguarding, and we would urge all medical men to familiarize themselves with these important requirements. The Department actually issued these regulations during the war, and we drew attention to them in 1941 and 1942 (this *Journal*, **45**: 163, and **46**: 273) but it was realized that the shortage of materials prevented the instalment of this protection then. Now, however, material is available and owners of this apparatus are required to instal the proper protection before January 1, 1948. The Department will give advice and will test and inspect the equipment on request. It will also say whether new equipment complies with regulations or not.

I esteem a habit of benignity greatly preferable to munificence. The former is peculiar to great and distinguished persons; the latter belongs to flatterers of the people, who tickle the levity of the multitude with a kind of pleasure.—Cicero.

MEN and BOOKS

LINNAEUS—BOTANIST AND PHYSICIAN*

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When the day of the schoolmen was nearing its end, medicine, philosophy and theology were in a condition of frozen thought. The spiders spun their webs over the great bundles of dried plants so carefully gathered by patient collectors from all over the world, and beetles were rapidly changing the specimens to dust. The confused scientists looked for some master whose touch could bring order out of chaos; who could change concrete disorder into the Platonic soul of abstraction and generalization, and break the ghostly tyranny of Aristotle.

The most unlikely place in the whole world where this Messiah would be found, was poor, inaccessible Sweden, her frugal people anæmic from the war debts of a megalomaniac king. While the world waited, a midwife in a little red cottage near Rashult, in Southern Sweden, came out of the bedroom and announced to the curate of the parish that his first born was a man child. Astrologers said the young son was under the constellation of Aries, but there was no full moon to retard his passage through the pubic arch. The midwife and the female relatives put a silver dollar in the bath to enrich him, a piece of steel in the cradle to prevent baby-snatching and a leaf torn from a hymn book to keep the devil away, while the father looked disapproval, but said nothing.

This was on May 13, 1707, the year that saw the union of England and Scotland, and which was followed by an epidemic of influenza, which, if we are to believe the Reverend Patrick Walker, was caused by the presence in Scotland of the "peoples of the abominations" (English). There was no silver spoon for the little Carl Linnaeus, but he held in his hand an invisible, golden key.

Shortly after Carl was born, his father became perpetual rector of the Lutheran parish and moved to Stenbrohult on Lake Möcklen, where he was able to give full play to his hobbies of gardening and botany. There is little to distract the country man, living in a mountain village, from the contemplation of the eternal. His whole existence is made up of alternating seasons and the steady movement between life and death. No wonder then, that the little boy, brought up under such conditions, retained to the end of his days, deep religious convictions. He seems also to have escaped the feverish paroxysms of doubt that so often beset the intellectual adolescent. With both parents passionately proud of their garden, Carl's love of flowers began with his mother's milk and

* Part of paper read before the Medical and Historical Club, Toronto, February 17, 1947.

continued with increasing ardour to the end of his life. At four, he was lisping the long names of the many rare plants in his father's garden collection. No fairer spot could be found for training a botanist than Stenbrohult, with its hills and valleys and its dark forest coming close to the rectory door. The lovely companions of singing birds, buds and blossoms, and the shining waters of the beautiful Lake Möcklen, nearly two miles long, gave Carl a childhood which he remembered with pleasure all his life. In his spare time the "little botanist" was wandering about in search of plants, learning unconsciously that wonder is the beginning of wisdom. Probably when he returned home with his hands full of "weeds", the kind neighbour women cautioned his mother that he was "not just quite right".

As he reached the gymnasium and began to mix with other boys, he set his heart on becoming a naturalist, and because there was only one way of doing such a thing in the college curricula of that time, he chose the faculty of medicine. However, his orthodox mother, like so many other women both before and after the Reformation, had from his birth sanctified him for a priest. As a compromise, the boy was sent to the University of Lund, where the syllabus, drawn up by fundamentalist divines who believed the earth was flat, was enough to disgust any bright boy; so in a short time, much to his mother's disappointment, Carl was off to Uppsala, three hundred miles away, and near the sinful city of Stockholm. Her displeasure was partly responsible for a decrease in Carl's money, and as he went about the wet streets with bark soles in his worn-out shoes, the boy was to know for the first time, the real pinch of poverty. Furthermore, the university at Uppsala was little improvement on Lund. There was, it is true, a theatre for anatomy, but no cadavers and no one to demonstrate. Linnaeus, however, went to Stockholm to see a public dissection of a woman who had been hanged, an event of such importance that the faculty made great preparations and even wrote the King for temporary postponement of the hanging in order that the anatomists might make the most out of it. This trip cost Linnaeus his last cent, and recalls the courage of young Vesalius, on moonlight nights fighting with savage dogs beneath the gibbets of Montfancon for the bones of criminals.

On a bleak day in April while he was sitting on a bench in the botanic garden, one of those benevolent old gentlemen who appear only in fairy tales, sat down beside him and asked about the notes he was making on some flowers in his hand. This was Linnaeus's introduction to one of the greatest scientists in Sweden, Olaf Celsius, dean of the University, whose name is famous because of his improvement of the thermometer. The result of that pleasant conversation in the garden was that Linnaeus was taken into the dean's home and given free access to one of the best libraries in Sweden. Celsius also procured a scholarship for him and made him a demonstrator in botany.

Now that he had more bodily comforts, he turned his active mind to some thoughts on botany that had come to him in the cold, sleepless nights. These he wrote out in book form, under the title "Preliminarie of Plants" and laid it on the desk of Celsius on New Year's Day 1730. Here Rudbeck, one of the world's greatest botanists at that period, found it and recognized at once that Linnaeus was a genius. He took him under his care, gave him the run of his library and a good salary as a tutor.

When Rudbeck was a young man, thirty-seven years ago, he had visited Lapland and ever since had cherished the desire to go back some day to make a complete survey of the natural history of that cold and forbidding Swedish province which was practically unknown. The great Uppsala fire (1702) had destroyed his collections before they had been properly studied. Now, with a promising young scholar, he could go again, this time vicariously. His prestige in the university made it comparatively easy to obtain some of the required money from the Royal Society, and on May 12, 1732, Linnaeus set off alone to Lapland and the midnight sun, on a hazardous and difficult expedition which more than anything else, set his feet firmly on the ladder of success.

When he left Uppsala,

> "Spring proclaimed from field and woodland glade
> Approach of Flora's cavalcade."

The early spring flowers were in bloom and the trees showed their first green. The stately, patient pines gave him grave company as his pace northward kept up with the sun, and he was able to note a great many plants at their best, some of which had never been described. Through cold, snow and heavy rains, wading at one time seven miles in marsh where the snow was unmelted, plagued with mosquitoes and other biting insects, he despondently recorded in his diary, "No parson could describe a worse hell than this". As he staggered along hunger was always running parallel with him. Some times he was able to catch fish; at the darkest hour he had to eat maggots. Once his boat split and he lost his birdskins, but fortunately for science, he saved his Journal, which is now carefully preserved at Uppsala. At last he reached the sea, when the summer was in full splendor, and the land seemed a miniature garden. As he rested his weary body, he studied botany and zoology, and gorged himself with fresh food, cow's milk and wild strawberries. Here in Boreas, the abode of the north wind, he saw the midnight sun for the first time, and probably looked upon the wonderful displays of the aurora borealis, which of course were not new to him. The

Lapps likened the sound which sometimes accompanied this phenomenon to the crackling of the joints of a herd of reindeer in the distance.

On the road home he investigated an endemic and fatal cattle sickness which he found was caused by the water hemlock (*cicuta virosa*) and suggested the remedy, which was to pull up all the plants. In the villages he noted the customs, dress and language of the natives, and recorded as did the Jesuits among the American Indians, that the Laplanders lacked cleanliness and that their primitive dwellings swarmed with flies.

He reached Uppsala on October 10, having travelled 4,793 English miles, 996 of them on foot. Saddest of all, he had spent the fifty dollars which was all the Royal Society had in the treasury, and was still in debt to the tune of eighty dollars. But in spite of his meagre equipment, he brought back with him a record of observations and a collection of plants, minerals and ethnological curiosities, that, under the conditions of transportation, was truly remarkable. Among the plants he found and described was the Twin-flower, always his favourite, and which, a few years later, when the binomial system of names was in use, was called by Gronovius *Linnaeus borealis*. He noted also that the common hairy-cap moss, *Polytrichum commune* (which also grows abundantly in Canada) made a good coverlet and pillow, and had the added virtue of keeping off the fleas. On November 9 he presented his report to the Royal Society, who received it with great delight.

After the Lapland journey he returned to the university for two more years. Because of the condition of the hospital, financial and otherwise, clinical instruction had been suspended. The other lectures were of little interest to him, so he spent all his time in scientific research and in teaching natural history to other students, usually gratis. In these years he finished fourteen memoirs, chiefly on botanical subjects. His private tutoring was so popular that toward spring, he had twenty students who paid him a total of twenty dollars, not enough to get him out of debt for his Lapland journey. Later he formed classes on a new and popular subject, assaying, receiving for this about seventy-five dollars. Weary of his academic work, he made a visit to Falun, a copper-mining centre in southern Sweden, dating from 1288, from which he wrote "I have enjoyed myself very well". This was to prove another landmark in his life for had he not fallen in love with the young maiden he met there for the first time, he would certainly never have remained in Sweden. On returning in March to Uppsala, he gave lectures on general botany, and on dietetics.

But the uncertainty of his future greatly depressed him. He was now twenty-seven years old and had been a student for seven years. Should he continue in this poorly-paid position he now held, or should he proceed to his medical doctorate and take up the practice of his profession? While he carefully weighed each in the balance, he was cautious enough to prepare a paper which he might use for a thesis when required. The title was "A new hypothesis as the cause of intermittent fever", in which he advanced some views that would shock the conservative members of the examining board. He had also many other manuscripts but was unable to find a publisher in Sweden. If he went to Holland he had a fair chance of getting them printed. At the same time he could obtain his M.D., but where was the money to come from?

At this crisis in his life, fortune again favoured him. The Governor of Dalecarlia commissioned him to conduct a scientific survey of the province. On July 3, 1734, Linnaeus left Falun for six weeks, and over rock-stabbed, timbered hills, under ceaseless difficulties of food and shelter, plagued by black flies and constant rain, he examined the silver mines, agriculture and quarries, and made collections of flowers and animals. In the grindstone quarries he found few workmen who lived to forty. One Sunday at church he saw two old men, but one was the village tailor and the other the cobbler. The forests were neglected, for the trees were felled solely for their inner bark, which they used as food for man and beast. He found the farmer who was the first in the province to plant potatoes, sharing them with his neighbours as a change from bark-bread. The place was so backward that the country folk were still using Runic letters.

His flower collections were very disappointing after Lapland. Only one new flower, a bladder-wort, was entered on his list of "finds"; one insect, and one bird, probably our Arctic three-toed woodpecker, which Linnaeus named and described. Among the articles used for food he noted that they salted down "blood lymph" when they slaughtered their animals, and then buried it in the forest for winter use. His nose was often offended in his travels, but never more so than when attending church, where the women chewed a garlic gum.

For a short time after his return to Falun, he gave courses on assaying and he also practiced medicine. In December 1734 he returned to Uppsala to get the necessaries for travelling abroad for his degree. The most important part, next to money, was an examination in Divinity, without which no one could obtain a passport.

Before leaving for his foreign travels he went back to spend Christmas at Falun, and to see the eighteen-year old Sara Elizabeth Moraea who had aroused his emotions on his last visit. On January 20 he asked the parents for her hand. Although her father was favourably impressed with the remarkable ability of young Carl, he nevertheless stipulated there should be

no wedding for three years. Carl spent another month with the Moraea family, receiving presents and congratulations, and left their home on February 20 with a contribution from Dr. Moraea as a token of his affection, and a little purse from his betrothed. After a month at his own home to comfort his father, grieving over the loss of his wife, he sailed from Sweden on April 19 as an unknown student, to return three years later a renowned scientist.

Travelling at this period was slow and he had much time to visit many places and local scientists. Not until June 2 did he reach Amsterdam, and on the 7th he crossed over to Hardervijk to be examined in general medicine. He produced the thesis he had already prepared at Uppsala, in which he maintained the theory that the cause of intermittent fever (malaria) in Sweden was the drinking of clayey water. The examiners seemed highly satisfied and granted his diploma on the 24th.

At this time the venerable Herman Boerhaave (1688-1738) was the chief medical oracle of Europe. He was also eminent in chemistry and botany, and Osler has called him the Dutch Hippocrates. When Boerhaave was exhausted in his consulting room, he refreshed his mind by working in his arboretum, where grew every kind of tree which would stand the rigorous climate of Holland. In 1736, the time of Linnaeus's visit, the old patriarch had decreased his medical consultations, admitting only a few patients. Knowing that Boerhaave was deeply versed in botany, Linnaeus tried to see him, but was unsuccessful. Gronovius, however, advised Linnaeus to write a letter. A few days later Boerhaave received him with great kindness, and took him out to the famous garden "a paradise, Holland's miracle, whose like no mortal can imagine", where grew a tree supposed never to have been described. Linnaeus recognized it as a variety of the mountain ash, the White Beam, growing abundantly in Sweden. The result of this meeting was a deep friendship for the few years left to the noble and generous physician, who proposed to send Linnaeus at once to the Cape, or to Surinam or even to America.

Through the efforts of his kind and influential friends, particularly Boerhaave, he was put in charge of a marvellous collection of plants and animals, gathered together by a very wealthy man, George Clifford, a director of the Dutch East India Company, and here he spent two years in naming and classifying the material. Clifford was so pleased that he sent Linnaeus to England where he met Hans Sloane, and many other English botanists, some of whom were strongly opposed to the new system of binomial nomenclature.

But although he had, through the generosity of Clifford, all the material things one could desire, a grand home, a carriage and servants, offers of a larger salary and a professorate, even a marriage to Boerhaave's daughter and a dowry of a million gulder, he rejected them all. The arrow that Cupid shot had taken such effect that he must return to the land of his birth. And besides, he had learned that Browallius, a scientist of no mean proportions, was casting glances at Lisa.

Just when he was ready for the journey home, he went down with typhoid, to be followed by cholera, from which he nearly died. Clifford kindly took him back to his house for another two months till he was able to travel.

In the two and a half years he was at Leyden he published twelve or fourteen larger works, besides smaller treatises, "a great testimony to a power of work and untiring industry which must awaken unstinted praise". Gronovius stood by him on every occasion and saw these books through the press.

He left Leyden in May, spent a month on the journey home, through Brussels and Paris, and then took the shortest route to Stenbrohult, "to tumble into his father's arms all the many volumes he had written and printed in Holland". At Falun, Dr. Moraea advised him to establish himself in practice before marrying Elsa. So Carl selected Stockholm, the largest city, as the place where he could most quickly gather together enough money to keep his wife in the style she was accustomed to.

When he arrived in the capital city (September, 1738) so deeply was he affected with lovesickness that he resolved to refrain from all writing and to let his botany rest while he turned his energies to medical practice, so that he might fulfil his promise to his father-in-law, who sometimes appeared to him as cruel as Laban. From seven in the morning to eight at night he worked among his patients, with hardly time to eat, and no time at all for social functions. He often saw from forty to sixty patients a day. He gained such a reputation among the laity for his treatment of chest disorders, that on one occasion a court lady with a cough called on him for advice. The pastilles of tragacanth he gave her relieved her so much that she carried them about in her purse. While playing cards with Queen Eleanora, the lady had occasion to use one of these lozenges and to explain how satisfactory they were. The result was that Linnaeus was called to the palace.

His private practice and his service in the naval hospital with always one to two hundred sick, and which he administered almost alone, would have kept an ordinary man very busy; but he began a garden to raise medicinal plants. From the opportunities he had for autopsies, he became the first pathological anatomist in that part of Europe. He still continued his lectures in botany and mineralogy to crowded classes, often as many as four hundred, and in summer he headed his students on field excursions. In 1739, he took a short holiday to go to Falun and claim his bride, whom he married on June 26.

His first year in the Academy took up a great deal of "spare time", but was very fruitful in its results. He made a catalogue of plants

which might be serviceable as drugs, and gave his presidential address on "Curiosities in Insects". As the months rolled by, however, he found that his energy was not enough to keep pace with his astonishing activity. The monotony of such heavy medical responsibilities became an oppressive burden, and he set his eyes on a position as a university teacher, preferably on the medical faculty at Uppsala. There were two professors filling the chairs, both very old and academically inactive, but both protested vehemently that they were as fit as fiddles. Rudbeck, however, died at eighty, in May of 1740, and Roberg resigned in July. Then began such scandalous squabbling and disgraceful lobbying that the university was in turmoil. One of the applicants for the position filed, as his required thesis, a slanderous attack on Linnaeus and his new nomenclature. On the day appointed for the disputation, which was in Latin, the auditorium was crowded with students who put on a row quite equal to anything in modern days. After some hours of "rough house" and coarse Latin abuse, the meeting ended with no appointment made. Three months later the chancellor of the university, weary of the indecision of the Consistory, asked the King to appoint Linnaeus Professor of Practical Medicine and Botany.

A few days after his appointment Linnaeus accepted a commission from the Government and the Swedish Parliament to investigate the natural productions of certain parts of south Sweden, returning to Stockholm at the end of August. In October he removed to Uppsala, glad to be rid of his "wretched practice" and there to remain for the rest of his days. He never attended a patient again.

And now, aged thirty-three and a half, he stands on the platform of the university hall to deliver his first lecture in Uppsala. With his theological training, he might have taken as his text, "It is the glory of God" says Solomon, "to conceal a thing: but the honour of kings is to search out a matter". He chose, however; "The discoveries that could be made from natural history travels in Sweden". He began at once his courses in Medicine, Anatomy and Physiology, in all of which he felt his lack of proper training. In another department, Rosen, a thoroughly grounded physician, taught Botany, Chemistry, Dietetics and Materia Medica, in none of which he was deeply interested. The Consistory quickly noted this, and a few months later (January 1742) suggested an exchange of chairs, and thus Linnaeus attained the place he had so long desired.

From 1741 to 1776 he never missed a lecture. His boundless energy made him weary of holidays, so he gave many extra courses. His class room was the largest hall obtainable, but some of his audience even then, had to stand. One reason for this was that botany was compulsory in Medicine and in Divinity and at one time the two faculties numbered about fifteen hundred students. Those in Divinity had to take botany because many of them would spend their lives in sparsely settled communities where an elementary knowledge of plants was necessary. But it was the charming personality of the lecturer, his interest and enthusiasm, his wonderful memory, his easy and delightful humour that produced frequent laughs and kept the seats at a premium. Humour is an essential ingredient of living and there is no reason why a teacher should be deprived of it. Although he spoke Swedish with the accent of the province in which he was born, he was so much a master of his department, so fluent and dramatic in his presentation, charging dry subjects with intellectual excitement, that the fame of his extraordinary power of teaching raised this unpretentious Swedish town to a Mecca for students from distant lands. When critics found fault with his weakness in Latin, in which the lectures were delivered, he replied *"Malo tres alapsas a Prisciano quam unam a Natura"* (Better three slaps in the face from Priscian, the noted Latin grammarian, than one from Nature).

In appearance, he was rather short and muscular, but not fat, weighing in his prime, 178 pounds. He had a high forehead, brown hair and quick, fiery, brown eyes. His walk was easy, rapid and lively, and he was always well dressed. Although he rose early, he rested when tired and could sleep at will, so soundly that he snored. He had what he called "an understanding throat, so I can digest anything, or go without". With such a physical make-up, one could surmise that he was quick to anger, but quickly cooled. As a practising physician he had great compassion for the sick, particularly little children. His ardent piety and his Lutheran upbringing made him believe in "Nemesis divina"—that God punishes transgression; but he did not assert that everything the orthodox divines taught was indisputable. Although he considered the Bible his main source of information, even in natural science, he often interpreted passages in his own way. He doubted the universal flood, he looked askance at Bishop Usher's guess of six thousand years since creation, and he believed that the elements existed before the Mosaic account. Of course, some of the orthodox quoted *"Ibi tres medici, ubi duo athei"*.

When he was at the meridian of his life, he could accomplish an enormous amount of work. In the summer he rose while the morning glory was opening (four a.m.). At six he breakfasted with pupils, then lectured informally till ten. Following this came his university work and his research, always heavy, till dinner time with his family. In the evening he strolled in the garden, planning new ventures and studying his new plants. Later he might visit his favourite pupils, like the brilliant Kuhn or Fabricius the

Dane, who was called the Linnaeus of entomology; promising to stay only half an hour but remaining till midnight. This was perhaps the happiest part of his day for it is recorded that his merry laugh rang loud and his face, between puffs of his pipe, beamed rosy red with enjoyment, plainly showing how much his soul longed for society and intimacy. Never was there the slightest trace of pomposity or patronizing.

On Sunday afternoons in the summer he was fond of mingling with the young people who gathered at Hammerby, his home in later years, just outside Uppsala. Sometimes he joined in the music and dancing and on one occasion he took part in a game of blind man's buff, in which Queen Louise, sister of Friedrich der Grosse was one of the players, and as such, was not supposed to be caught. Imagine the consternation of the circle when Linnaeus who was "It" touched her on the shoulder, at which she called out "It is I", whereupon Linnaeus said "Clap, woman! Who plays at this game may expect to be caught".

His Illnesses

From early life he had severe attacks of migraine, sometimes lasting a whole day. The pains he had in his joints, and which he considered due to gout, were relieved by eating strawberries. "Every year" he wrote "I eat as many as my stomach will hold". Since few other physicians have found strawberries an effective remedy for gout, there may be some reason for doubting the diagnosis. In 1740 and again in 1750, he was in bed for some weeks with "angina" the name in that day given to any severe dyspnœa. In some of these attacks he was near suffocation. In 1756 his ill-health for a few weeks was attributed to scurvy. To cure it, he gave up coffee for a whole month, a severe deprivation, for, like most northern people, Linnaeus drank it in large quantities. When this social habit was new in Sweden it was unfavourably compared to tea. Certain savants proved to their own satisfaction that on the Judgment Day, all coffee-drinkers would rise from the grave as black as coffee-grounds. Gustavus Adolphus did not depend upon his physicians and determined to find out for himself by experiment. As King, he had some advantages over the ordinary research worker who is dependent upon animals. Twin brothers had been condemned to death. They were given "fatal doses", which physicians predicted would cause death rapidly, one receiving tea and the other coffee. Neither died, so they were given larger portions each day, and a medical commission watched them. But the doctors died and the brothers lived merrily on at the State's charge. Finally, the tea drinker died at the age of eighty-three. Probably the experiment ended there, for there is no record of the other brother. When Voltaire, a passionate coffee addict himself heard the story years afterwards, he commented; "Coffee is a deadly poison, but it acts very slowly". He himself at eighty-four travelled from Switzerland to Paris to see the opening of one of his plays.

As his birthdays flew rapidly by, his exhausting work and the burden of years began to tell on Linnaeus, and his sympathies moved more slowly. At sixty-five he lost the last of his teeth and his hearing was so impaired that he could no longer recognize the bird songs which had been a life-long pleasure. Even in summer he felt the comfort of a fire. He often had vertigo when he bent over and he told Back, his physician, that his end was approaching. The medical advice of diet, rest and bleeding was rejected. If he gave up lecturing, he said, it would make him forget things and render him dumb. In another term he might forget his own name. Doctors in that age took medical advice from their confrères no better than they do today. The proverbial absent-mindedness so frequently associated with professors, now became marked. It was quite a common thing for him, when visiting, to leave behind his night-cap and carry home his host's overcoat.

In 1774 when lecturing in private he had his first stroke, and for some time he could not raise himself from his chair. Next year, at sixty-eight, feeling his incipient dotage, he asked for release from lecturing, because "I am old and tottering, can hardly bear the autumn cold, and I am toothless, so it is hard for me to talk". Early in 1776 the penumbra of death was apparent; the slow deterioration was becoming more marked; he shuffled along, talked confusedly and could scarcely write. A few months later, after two more strokes, one of which paralyzed his right side, he asked for an appointment as Professor Emeritus with salary and his request was granted. He appeared for a time a little better, as he smoked his pipe with seeming enjoyment, and even went for short drives inside the town. In December he persuaded the coachman to go three miles in the country. When they did not return, the searchers found him in a peasant's house chilled to the bone. The slow, lingering, obstinate struggle with death ended on January 10, 1777, when, with his favourite pupil, the English Rotherman at his side, he fell asleep like a man, the excess of whose labours are a ready passport to the blessings of repose.

Several years before the long night had begun to close in upon him, he wrote directions for his funeral. "Put me in a coffin, unshaved, unwashed, unclad. Wrap me in a sheet and close the coffin at once, so no one may see my wretchedness. Let the great bell be tolled, but none other. . . . Entertain nobody at my funeral."

In the dark, still evening of January 22, "many doctors", all once his pupils, raised to

their shoulders the body of their beloved teacher and passed with measured tread along the cobbled street. Lanterns and smoky torches lighted the way, and the majestic tolling of the cathedral bell added its note of solemnity and sorrow. In the vaulted church, dimly lit by flickering candles, the organ took up the litany of the dead and the venerable Dean, eighty-three years old, read the simple burial service. The coffin was lowered with solemn rites to the walled-in grave under the organ loft and the grave at once closed down.

The notifications that were sent out for the funeral had been prepared beforehand by Linnaeus himself. On the day after the funeral however, the widow disregarding his written orders, provided an ample dinner for a great number of those attending the services.

The Academy of Science, of which he had been a founder and the first President, asked Archiater Back, who had been his friend and physician, to deliver the memorial oration, which he did in December, "before the King and a numerous auditory". When the Parliament met in October, the King, Gustaf III, referred to Linnaeus in these words: "But I have lost, alas, a man whose celebrity was as great all over the world as the honour was bright which his country derived from him as a citizen. Long will Uppsala remember the celebrity which it acquired by the name of Linnaeus."

HIS PLACE IN SCIENCE

And now what judgment can we form of this the last of the schoolmen and last of the great theological observers of nature, dead more than a century and a half? When he came on the scene, the academical air was clouded by the hair-splitting interpretation of Aristotle or the biblical Hebrew and Greek texts. A museum was a place where dried crocodiles were kept or the little Scotch boy's brother who "had twa heads and was in a bottle". When Linnaeus died there was a new and scientific interest in collecting in all parts of the world, stimulated by a system of classification based on relationship. By an Ariadnean thread, he had led natural history out of the jungle in which primitive man entertains the notions of things. He had reformed the art of description and left models of clearness which get down to the very marrow and pope's nose of the subject in hand. And he was fortunate to live long enough to see his classification adopted in Sweden and in England (1760).

To about 8,000 plants he gave not only new names, but new descriptions, separating the essential from the non-essential, adding critical remarks on their names by old authors, their countries, occurrence, etc. Since he died the number of known species has increased out of all bounds. Merrill, in forty-two years in the East Indies, described over 4,000 new plants; by 1946 it has been estimated that there are 45,000 species in the lands and islands washed by the Pacific. During the war, the American botanists scouting for quinine, thought that there were at least 10,000 unnamed plants growing on the west slope of the Andes. The Index Kewensis which attempted to list all flowering plants known in 1892-95, had 375,000 names.

But Linnaeus recognized that plant naming was not the highest attainment. He laid down lines of geographical distribution, studied the miracle of fertilization, the winter sleep of plants, the formation of buds and was the first to discover the nectaries and suggest their function. He also made the first successful attempt at hybridization.

Nor was he without mistakes, but because of a sanity refreshing as the wind that blows, and an incorrigible honesty, to use Lamb's pleasant phrase, he was quick to correct them. These errors however were very rare, and sometimes caused a smile. From America came a specimen of a shrub commonly called here "leather wood" or "moose wood" (*Dirca palustris*). Linnaeus evidently had never heard of a moose and thought it must be "mouse wood". He let his keen imagination have full play when he gave it a Latin name, *Dirca,* after the wife of Lycus. She was murdered by her husband who tied her to the horns of a bull. Afterwards Jupiter transformed her into a fountain.

To medicine he gave the improvement of the thermometer. Celsus showed him in those days when he was so hungry and unhappy, an adaptation of Fahrenheit's instrument, with the calibration from 100 (freezing point) to 0 boiling point. Linnaeus suggested the reverse order and so it is today.

He raised his voice with no uncertain sound against unnecessary bleeding, and was the father of simple prescribing. "He who writes long prescriptions" he noted, "does so either from ignorance or with a desire to swindle." Add to all these accomplishments that he was the first Swedish ethnologist, the first to teach medicine at the bedside, the founder of crystallography, and that he laid the corner stone of a geological system, and one can see why his memory is still held in reverence by the whole scientific world. He was born a man of method and his genius lay in his enormous capability of work. His humble simplicity prevented success from going to his head. "I am only like a grindstone which sharpens but is not able to cut"; and he considered "honours empty nuts and titles, wind". In small things and in great, he showed himself "an unsurpassed master in bringing order, light and system where ignorance and indifference had produced obscurity and confusion". In his unceasing worship of the Flower goddess he wore no dull leaden mask of idle curiosity. He wanted only, like John Hunter, to study life in all its manifestations; and thus he lengthened the perspective of science and attained immortality.

Throughout his long life he never lost sight of the fact that the study of nature is ever closely knit with the beautiful and the sublime.

"One impulse from a vernal wood
May teach you more of man,
Of mortal evil or of good
Than all the sages can."

ASSOCIATION NOTES

Welcome to Winnipeg

"Sir, you are very welcome at our house;
It must appear in other ways than words
Therefore I scant this breathing courtesy."

Here in Winnipeg we are very busy getting ready to entertain you. There is, as you can imagine, much to be done but we are all doing it, and doing it in the pleasurable anticipation of meeting you. You have been promised that a "Western Welcome" awaits you and we shall be as good as our word.

Perhaps some of you may think that "Western Welcome" is merely a slogan, and that geography can have little to do with hospitality. But there are a number of reasons why our mode of life should give an individuality to our way of greeting and entertaining strangers. Within the memories of men still living ours was a small town separated from its still smaller neighbours by great distances. New faces were not often seen and as a consequence strangers were more than welcome. The simple manners of the people quickly placed the visitor at ease and made him feel at home. We are not far removed from these days and the tradition of hospitality is still strong. We accept it as a duty but practise it as a pleasure.

There are other reasons why warm welcomes are here the rule. The sun which shines so brightly for so many hours of so many days each year quickly thaws the coolness which ordinarily exists between strangers. And the prairies upon which the city stands give a sense of freedom and a largeness of view not possible when a community is hedged in by forests or walled in by mountains. Moreover, our city is too young for time to have settled its society into strata and as a result all meet on equal terms. The citizens, lay and professional, remembering the friendliness which greeted them when they were strangers feel it is their duty to show similar hospitality to the newcomers today.

These are among the reasons why "Western Welcome" is more than a mere slogan. There is in our way of life a spontaneity, a frankness and a freedom from restraint that influences our behaviour towards strangers.

Attendance at Conventions is primarily for the purpose of getting first hand information on recent advances in our work but of equal importance is the opportunity it affords of

(Courtesy, Manitoba Government Travel and Publicity Bureau)

Parliament Buildings, Winnipeg

getting that change which is as good as a rest. Excellent arrangements are being made for the scientific meetings and the holiday aspect of your stay is being looked after with equal thoroughness. There are many golf courses over which you can play. Entertainments are being planned both for the doctors and their wives. All the facilities that the city can offer and that you can enjoy will be at your disposal. Later on the entertainment program will be given in greater detail. We trust that when you read it, it will be with a view of participation.

We hope that very many of you will be our guests this year. To say we bid you welcome is as far as words can go but "There is an emanation from the heart in genuine hospitality which cannot be described but is immediately felt and puts the stranger at once at his ease." So will you find it in Winnipeg. J.C.H.

Alberta University Alumni

The Alberta University Alumni will meet for dinner at 6.30 p.m. Thursday, June 26, at the Fort Garry Hotel.

PRELIMINARY PROGRAM
SEVENTY-EIGHTH ANNUAL MEETING
of the

Canadian Medical Association

TO BE HELD IN THE ROYAL ALEXANDRA HOTEL, WINNIPEG
JUNE 23, 24, 25, 26, 27, 1947

President - - - -	DR. WALLACE WILSON, Vancouver
President-Elect - - -	DR. F. G. MCGUINNESS, Winnipeg
General Secretary - - -	DR. T. C. ROUTLEY, Toronto
Assistant Secretary - -	DR. A. D. KELLY, Toronto
Local Hon. Secretary, Committee on Arrangements	DR. D. L. SCOTT, Winnipeg

Detailed arrangements for the Seventy-eighth Annual Meeting to be held in Winnipeg during the week of June 23 are proceeding satisfactorily.

General Council will meet on Monday and Tuesday, June 23 and 24.

On Tuesday evening, the members of General Council will be dinner guests of the Manitoba Division.

A series of Round Table Conferences has been arranged for the mornings of Wednesday, Thursday and Friday, from nine until ten thirty o'clock to be followed by General Sessions.

Sectional Meetings will be held on Wednesday, Thursday and Friday afternoons.

The Annual General Meeting will be held on Wednesday evening, June 25, commencing at 8.30 o'clock. On this occasion, the retiring President, Dr. Wallace Wilson, will hand over the badge of office to his successor Dr. F. G. McGuinness.

A panel discussion on the provision of medical care is being arranged for Thursday evening, June 26, by the Committee on Medical Economics under the chairmanship of Dr. G. F. Strong of Vancouver.

OTHER MEETINGS

The Manitoba Division will hold its annual business meeting on Tuesday afternoon, June 24.

The Grand Council of the Canadian Cancer Society will meet in the Royal Alexandra Hotel, Winnipeg, on Saturday, Sunday and Monday, June 21, 22 and 23, commencing at 9.30 a.m.

The Royal College of Physicians and Surgeons of Canada will hold the following meetings in the Royal Alexandra Hotel, Winnipeg.

Monday, June 23—at 11.00 a.m.—Meeting of Executive Committee.

Tuesday, June 24—at 9.00 a.m.—Meeting of Council, continuing all day and during the evening.

The Canadian Society of Allergists will hold its annual meeting in the Royal Alexandra Hotel, Winnipeg, on Tuesday, June 24, the morning session taking the form of a Round Table discussion on "Asthma" with the following taking part:

DR. H. K. DETWEILER, Toronto (*Chairman*)
DR. C. H. A. WALTON, Winnipeg
DR. A. T. HENDERSON, Montreal
DR. J. R. ROSS, Toronto

This will be followed by a business session, with a scientific session in the afternoon.

The fifth annual meeting of the *Canadian Anæsthetists' Society* will be held on Wednesday, June 25, immediately following the session of the Section of Anæsthesia under whose auspices all scientific meetings are being held. The agenda will include the election of officers

and a discussion of tariff, certification, post-graduate education and any business presented by members. The annual dinner will be held on Thursday, June 26. Preceding this there will be business meetings of the various C.A.S. Provincial Divisions.

The Alberta University Medical Alumni will hold a dinner at the Fort Garry Hotel, Winnipeg, on Thursday, June 26, commencing at 6.30 p.m. All interested are invited.

The Canadian Medical Protective Association will meet at 4.30 p.m. on Wednesday, June 25.

The Canadian Association of Radiologists will meet in the Royal Alexandra Hotel on the afternoon and evening of Tuesday, June 24.

Federation of Medical Women of Canada.—The Council of the Federation of Medical Women of Canada will meet on Tuesday evening, June 24. The Annual Meeting will take the form of a breakfast at 8.30 a.m. on Wednesday, June 25, at the Business and Professional Women's Club, 3 Evergreen Place. Following the breakfast there will be a business session.

Registrars of the Colleges of Physicians and Surgeons.—The Registrars of the various Colleges of Physicians and Surgeons of Canada will meet at 2.00 p.m. on Thursday, June 26.

Canadian Urological Association.—The Canadian Urological Association will meet on Thursday, June 26, immediately following the afternoon session of the Section of Urology.

SCIENTIFIC PROGRAM

Wednesday, June 25

ROUND TABLE CONFERENCES

9.00 – 10.30 a.m.

Anæsthesia

Subject: *Anæsthesia for the Occasional Anæsthetist.*
Chairman: **Dr. D. C. Aikenhead, Winnipeg.**
Dr. Walter S. Johns, Calgary.
Dr. J. Brener, Winnipeg.
Dr. D. Huggins, Winnipeg.
Dr. D. Revell, Winnipeg.
Dr. E. Watts, Edmonton.

Dermatology

Subject: *Seborrhœic Dermatitis.*
Chairman: **Dr. Norman Wrong, Toronto.**

Medicine and Surgery

Subject: *The Management of Hypertension.*
Chairmen: **Dr. J. D. Adamson, Winnipeg and Dr. A. C. Abbott, Winnipeg.**

Obstetrics and Gynæcology

Subject: *Cæsarean Section—the indications and contraindications.*
Chairman: **Dr. W. P. Tew, London.**
Dr. G. M. White, Saint John.
Dr. A. B. Nash, Victoria.
Dr. F. G. McGuinness, Winnipeg.
Dr. L. Armstrong, Toronto.
Dr. J. S. Henry, Montreal.

Wednesday, June 25—*Continued*

Ophthalmology

Subject: *Ocular Injuries.*
Chairman: **Dr. N. L. Elvin, Winnipeg.**

Pædiatrics and Otolaryngology

Subject: *The Management of Bulbar Poliomyelitis.*
Chairman: **Dr. Harry Medovy, Winnipeg.**
Dr. E. J. Huenekens, Minneapolis.
Dr. R. E. Priest, Minneapolis.
Dr. A. B. Baker, Minneapolis.
Dr. Alan Ross, Montreal.
Dr. Robert Black, Winnipeg.

Psychiatry

Subject: *Treatment in D.V.A. Hospitals—Rehabilitation of Psychiatric cases, including experience with subshock, insulin, indications, mode of action, results, etc.*
Chairman: **Dr. W. M. Musgrove, Winnipeg.**
Dr. T. E. Dancey, Montreal.
Dr. Gordon Hutton, Vancouver.

Radiology

Subject: *Therapy—Roentgen Therapy in the Treatment of Arthritis.*
Chairman: **Dr. Ethlyn Trapp, Vancouver.**

GENERAL SESSION

Wednesday, June 25

10.45 a.m.

Valedictory Address.
Dr. Wallace Wilson, Vancouver.

The Osler Lecture—Osler: The Text-book and Medical Education.
Prof. J. M. McMichael, London.

The Early Diagnosis of Carcinoma of the Stomach.
Dr. Leo G. Rigler, Minneapolis.

SECTIONAL MEETINGS

Wednesday, June 25

2.15 p.m.

Section of Anæsthesia

Combined Anæsthesia.
Dr. R. Letienne, Winnipeg.

Anæsthesia in Chest Surgery.
Dr. J. A. Blezard, London.

Regional Anæsthesia.
Dr. John Carroll, Montreal.

Pentothal Anæsthesia.
Dr. Fernando Hudon, Quebec.

Section of Dermatology

Treatment of Malignant Skin Tumours.
Dr. George Brock, Winnipeg.

Recent Concepts of the Dermatoscleroses.
Dr. Paul O'Leary, Rochester.

Recent Advances in Dermatology.
Dr. Harold Orr, Edmonton.

Manifestations of Skin Sensitivity.
Dr. G. S. Williamson, Ottawa.

Skin Lesions of Functional Nervous Disease.
Dr. D. E. H. Cleveland, Vancouver.

Wednesday, June 25—*Continued*

Section of Medicine

Obscure Causes of Heart Failure.
Dr. Gerard Allison, Winnipeg.

Diagnosis in Arthritis and Rheumatism.
Dr. Douglas Taylor, Toronto.

Immunization Procedures in Acute Infections.
Dr. R. D. Defries, Toronto.

Minor Ailments.
Dr. Charles Hunter, Winnipeg.

Section of Ophthalmology

Tributary Retinal Venous Thrombosis.
Dr. Robert M. Ramsay, Winnipeg.

The Newer Types of Implants used after Enucleation.
Dr. J. S. Crawford, Toronto.

Toxoplasmic Chorioretinitis.
Dr. Kenneth B. Johnston, Montreal.

The Use of Orthoptics in the Practice of Ophthalmology.
Dr. Charles E. Davies, Vancouver.

Vertical Deviations.
Dr. James McGillivray, Winnipeg.

Section of Pædiatrics

Congenital Heart Disease.
(a) Diagnosis—**Dr. John Keith, Toronto.**
(b) Surgical Approach—**Dr. Gordon Murray, Toronto.**

Subdural Hæmatoma in Infants.
(a) Etiology and Diagnosis—**Dr. Taylor Statten, Toronto.**
(b) Surgical Approach—**Dr. Arthur Elvidge, Montreal.**

Electro Encephalography in Pædiatrics.
Dr. Harold Rice, Winnipeg.

Section of Radiology

The Value of Plain Abdominal Roentgenograms.
Dr. F. G. Stuart, Winnipeg.

Radiation Treatment in Carcinoma of the Fundus Uteri.
Dr. Ethlyn Trapp, Vancouver.

The Treatment of Angiomas.
Dr. Origene Dufresne, Montreal.

Calcification in the Ascending Aorta as a Roentgen Sign of Luetic Aortitis.
Dr. R. A. MacPherson, Winnipeg.

Section of Surgery

A Follow-up of the Treatment of Intervertebral Discs.
Dr. H. F. Cameron, Winnipeg.

Subject to be announced.
Dr. Warren H. Cole, Chicago.

Results of Surgical Treatment of Bronchiectasis.
Dr. F. J. Kergin, Toronto.

Intertrochanteric Fractures of the Femur, treated by Skeletal Fixation.
Dr. J. R. Naden, Vancouver.

Thursday, June 26

ROUND TABLE CONFERENCES

9.00 - 10.30 a.m.

Anæsthesia

Subject: *Anæsthesia for Chest Surgery.*
Chairman: **Dr. A. C. Rumball, Winnipeg.**
Dr. J. D. Cameron, Toronto.
Dr. Marjorie Bennett, Winnipeg.
Dr. F. Walton, Winnipeg.
Dr. J. M. McKinnon, Winnipeg.

Dermatology

Subject: *Furunculosis.*
Chairman: **Dr. A. R. Birt, Winnipeg.**

Medicine, Obstetrics and Gynæcology

Subject: *Endocrine Problems of Puberty, Reproduction and Menopause.*
Chairman: **Dr. H. B. VanWyck, Toronto.**
Dr. Willard Holmes, Saskatoon.
Dr. Stuart Henry, Montreal.

Otolaryngology

Subject: *Chronic Otitis Media and Mastoiditis.*
Chairman: **Dr. Robert Black, Winnipeg.**
Dr. Frank Macneil, Winnipeg.
Dr. T. J. Haughton, Regina.
Dr. I. H. Beckman, Winnipeg.
Dr. G. M. T. Hazen, Saskatoon.
Dr. E. J. Washington, Winnipeg.

Psychiatry

Subject: *Child Psychiatry.*
Chairman: **Dr. T. Alex Pincock, Winnipeg.**
Dr. G. M. Stephens, Winnipeg.
Dr. Brian Bird, Toronto.
Dr. C. G. Stogdill, Ottawa.

Radiology

Subject: *Diagnostic—Cardio-vascular Roentgenology.*
Chairman: **Dr. H. M. Edmison, Winnipeg.**
Dr. A. E. Childe, Winnipeg.
Dr. L. R. Coke, Winnipeg.
Dr. F. A. L. Mathewson, Winnipeg.
Dr. Harry Medovy, Winnipeg.

Surgery

Subject: *Vascular Disorders of the Lower Extremities.*
Chairman: **Dr. C. E. Corrigan, Winnipeg.**

Urology

Subject: *Anuria.*
Chairman: **Dr. H. D. Morse, Winnipeg.**
Dr. J. C. McClelland, Toronto.
Dr. Joseph Doupe, Winnipeg.
Dr. Daniel Nicholson, Winnipeg.

GENERAL SESSION

Thursday, June 26

10.45 a.m.

The Present Status of Penicillin in the Treatment of Syphilis.
Dr. Paul O'Leary, Rochester.

Subject to be announced.
Dr. Warren H. Cole, Chicago.

Psychotherapy in Medical Practice.
Dr. C. B. Farrar, Toronto.

SECTIONAL MEETINGS

Thursday, June 26

2.15 p.m.

Section of Anæsthesia

Anæsthesia in Major Abdominal Surgery; a comparative study of continuous spinal and cyclopropane with curare.
Dr. Dorothea M. Wardrop, Winnipeg.

Oxygen Saturation of the Blood in Several Types of Anæsthesia.
Dr. Stanley Campbell and
Dr. D. M. Bean, Toronto.

Anæsthesia for Ophthalmic Surgery.
Dr. E. H. Watts, Edmonton.

Hypobaric Pontocaine Spinal Anæsthesia for Exploration for Nucleus Pulposus.
Dr. Pierre C. Lund, Winnipeg.

Armed Forces Medical Section

The Field Surgical Unit.
Dr. J. A. B. Hillsman, Winnipeg.

Recent Advances in Aviation Medicine.
Dr. W. R. Franks, Toronto.

The Medical Aspects of Civil Defence.
Dr. O. M. Solandt, Ottawa.

Section of Medicine

The Rôle of Proteins in Management of Diabetes.
Dr. A. Hollenberg, Winnipeg.

The Treatment of Peptic Ulcer.
Dr. A. H. Gordon, Montreal.

Epilepsy, Tridione and results.
Dr. C. A. Gauthier, Quebec.

Enigmatic Anæmias.
Dr. William Magner, Toronto.

Section of Obstetrics and Gynæcology

Diabetes in Pregnancy.
Dr. W. P. Tew, London.

The Differential Diagnosis of Chronic Lower Abdominal Pain in the Adult Female.
Dr. Brian D. Best, Winnipeg.

Prolapse.
Dr. L. T. Armstrong, Toronto.

Blood Loss in Labour.
Dr. George White, Saint John.

Section of Otolaryngology

Epistaxis.
Dr. J. K. M. Dickie, Ottawa.

Clinical Application of Penicillin in Otolaryngology.
Dr. Keith Hutchison, Montreal.

Ménière's Disease, Diagnosis and Treatment.
Dr. P. E. Ireland, Toronto.

Thursday, June 26—*Continued*

Section of Radiology

Myelography—some Technical Considerations (diagnosis).
Dr. Harold Morison, Winnipeg.

Emphysema: An Early Sign of Bronchogenic Carcinoma.
Dr. Leo G. Rigler, Minneapolis.

The Relationship of Radiological Diagnosis to Radiotherapy in the Treatment of Carcinoma of the Breast.
Dr. W. A. Jones, Kingston.

Roentgen Therapy in Carcinoma of the Vulva.
Dr. Jean Bouchard and
Dr. Carleton B. Peirce, Montreal.

Pneumorthography of the Knee Joint.
Dr. Paul P. Hauch, London.

Section of Surgery

Subject to be announced.
Dr. M. B. Perrin, Winnipeg.

Carcinoma of the Left Colon.
Dr. Donald Campbell, Hamilton.

Early Diagnosis of Subdiaphragmatic Abscess by Artificial Pneumoperitoneum.
Dr. A. L. Wilkie, Montreal.

Subject to be announced.
Dr. C. Bisson, Montreal.

Section of Urology

Essential Hæmaturia.
Dr. D. R. Mitchell, Toronto.

Renal Cysts.
Dr. R. E. Powell, Montreal.

Sarcoma of the Kidney.
Dr. L. G. Wood, Vancouver.

Wilms' Tumours (review of cases).
Dr. Gordon Ellis, Edmonton.

Friday, June 27

ROUND TABLE CONFERENCES

9.00 – 10.30 a.m.

Dermatology

Subject: *Ringworm of the Scalp.*
Chairman: **Dr. A. M. Davidson, Winnipeg.**

Medicine

Subject: *The Management of Peptic Ulcer.*
Chairman: **Dr. J. Wendell Macleod, Winnipeg.**

Obstetrics and Pædiatrics

Subject: *The Rh Factor in Obstetrics and Pædiatrics.*
Chairman: **Dr. Bruce Chown, Winnipeg.**
Dr. Ronald Denton, Montreal.
Dr. Ross Vant, Edmonton.

Friday, June 27—*Continued*

Psychiatry

Subject: *Electro Encephalography in Psychiatry.*
Chairman: **Dr. G. L. Adamson, Winnipeg.**
Dr. John Kershman, Montreal.
Dr. Harold V. Rice, Winnipeg.
Dr. L. D. Proctor, Toronto.

Surgery

Subject: *Management of Intestinal Obstruction.*
Chairman: **Dr. M. R. MacCharles, Winnipeg.**
Dr. J. C. Armour, Montreal.
Dr. A. D. McLachlin, London.
Dr. R. A. Macpherson, Winnipeg.

Urology

Subject: *The Rôle of Antibiotics and Chemotherapy in Urology.*
Chairman: **Dr. J. C. McClelland, Toronto.**
Dr. D. R. Mitchell, Toronto.
Dr. C. M. Spooner, Toronto.
Dr. D. Swartz, Winnipeg.

GENERAL SESSION

Friday, June 27

10.45 a.m.

Medical Implications of Recent Developments in Atomic Physics.
Dr. A. Cipriani, Chalk River.

Some Practical Aspects of Recent Advances in Obstetrics and Gynæcology.
Dr. A. B. Nash, Victoria.

SECTIONAL MEETINGS

Friday, June 27

2.15 p.m.

Armed Forces Medical Section

Glimpses of the R.C.A.M.C. in Action.
Dr. Athol Gordon, Winnipeg.

The Sequelæ of Local Exposure to Cold.
Dr. D. R. Webster, Montreal.

Operation Crossroads (The Bikini Experiment).
Major General R. M. Luton, Ottawa.

Section of Historical Medicine

Milestones in Canadian Medicine.
Dr. Heber Jamieson, Edmonton.

Doctor C. E. Smythe, Pioneer Physician of Medicine Hat.
Dr. G. D. Stanley, Calgary.

A Boy's Eye View of the Doctors He knew, 1889 to 1896.
Dr. M. H. V. Cameron, Toronto.

Jeanne Mance.
Dr. H. E. MacDermot, Montreal.

Bucke's Travels.
Dr. Edwin Seaborn, London.

Friday, June 27—*Continued*

Section of Industrial Medicine

Workmen's Compensation.
Dr. D. J. Fraser, Winnipeg.

Accident Proneness.
Dr. G. E. Hobbs, London.

Organization and Experience of a Large Industrial Medical Department.
Dr. K. E. Dowd, Montreal.

Section of Medicine

Symposium—Recent Advances in Therapeutics.
Chairman and leader of discussion—
Dr. Ray Farquharson, Toronto.

Antibiotics—**Dr. S. R. Townsend, Montreal.**
Thiouracil—**Dr. John M. Kilgour, Winnipeg.**
Anticoagulants—**Dr. E. S. Mills, Montreal.**
Anti-histamine and Related Substances—
Dr. C. H. A. Walton, Winnipeg.
Folic Acid—**Dr. Ray Farquharson, Toronto.**
Nitrogen Mustards, B.A.L., etc.—
Dr. Athol Gordon, Winnipeg.

Section of Obstetrics and Gynæcology

Conduct of Trial of Labour.
Dr. A. W. Andison, Winnipeg.

Malignancy of the Vulva.
Dr. J. A. Brown, Regina.

The Management of Dysmenorrhœa.
Dr. J. O. Baker, Edmonton.

Section of Pædiatrics

Cœliac Disease.
Dr. F. W. Wiglesworth, Montreal.

Milk Allergy.
Dr. R. C. Browne, Fort William.

Epidemic Diarrhœas of Newborn Infants.
Dr. Murray McLandress, Winnipeg and
Dr. Maurice Berger, Winnipeg.

Section of Psychiatry

Functional Disorders of the Gastro-Intestinal System.
Dr. J. Wendell Macleod, Winnipeg.

Somatic Symptoms in the Psychoses.
Dr. Edward Johnson, Selkirk.

The Treatment of Psychosomatic Disorders.
Dr. Trevor Owen, Toronto.

Mental Hygiene Related to Psychosomatic Disorders.
Dr. George Stevenson, London.

Section of Surgery

Repair of Bony Defects of the Face and Jaws.
Dr. E. W. Pickard, Winnipeg.

Present Day Treatment of Hyperthyroidism.
Dr. Walter MacKenzie, Edmonton.

The Treatment of Perforated Peptic Ulcer.
Dr. D. L. C. Bingham, Kingston.

The Present Status of Vagus Section in Ulceration of the Stomach and Duodenum.
Dr. E. Bruce Tovee, Chicago.

Friday, June 27—*Continued*

Section of Urology

Ureteritis.
Dr. Earl Hall, Vancouver.

Repair of Postoperative Urinary Fistula of Unusual Type.
Dr. Hilton S. Good, Regina.

The Urologist and the General Practitioner.
Dr. W. P. Hogarth, Fort William.

Diverticula of the Bladder with case reports.
Dr. N. B. Berry, Kingston.

Consideration of Infected Bilateral Renal Calculi.
Dr. Albert G. Laroche, St. Hyacinthe.

TRAVELLING

The Canadian Passenger Association has authorized special convention rates by the use of Identification Certificates which may be obtained on application to the General Secretary. The arrangements are as follows:

DATES OF SALE

Western Canada — From British Columbia, Alberta, Saskatchewan, Manitoba, and Port Arthur, Armstrong and points west of these centres in Ontario,—June 14 to 23, inclusive.

Eastern Canada—From all points east of Port Arthur and Armstrong, June 13 to 22, inclusive.

FARE BASIS

Round trip tickets will be sold at the rate of fare and one-third current fares, plus 25 cents, upon presentation of Identification Certificates to ticket agents at time of purchase of tickets. Summer excursion fares, where on a lower basis than Convention fares, will also apply.

Return limit. — Thirty days in addition to date of sale. Passengers must reach original starting point not later than midnight of final return limit.

MEDICAL SOCIETIES

Defence Medical Association of Canada

The Military District No. 2 Branch of the Defence Medical Association of Canada held the March meeting at the former Eglinton Hunt Club, now the Institute of Aviation Medicine. A wild snowstorm kept most of the members home but about thirty got through the drifts and up the hills. The president, Col. M. H. Brown and Brig. G. Sinclair reported the Ottawa meeting.

Wing Commander W. R. Franks explained the Air Force research establishment and its liaison with civil aviation and the T.C.A. as well as its link with Defence Research. We recalled Banting's early efforts to get defence research started in Canada, and its remarkable growth.

After the business meeting Wing Commander Brock Brown showed us the research facilities of the Institute. We enjoyed the warmth of the 115 degrees room and cooled off in the 54 below zero chamber. We heard the noise a Canso flying boat makes when it takes off, then listened to the audiometer in a sound proof room. We watched the human centrifuge in action and examined the various types of Franks Flying Suits.

Finally we partook of the generous hospitality of the Officers' Mess. Wing Commander Brown promised a repetition of the invitation for a summer meeting.

LILLIAN A. CHASE

Toronto Academy of Medicine

The Toronto Academy of Medicine recently held a symposium on œdema. Dr. Donal P. Murnaghan, speaking on Pathogenesis and Clinical Significance of Cardiac Œdema, said that the simple theory of decreased movement of tissue fluids adapted from Starling's work is no longer accepted as a satisfactory explanation. Increase in blood volume, gain in weight and œdema occur before there is elevation of peripheral venous pressure, as ordinarily measured in the antecubital vein. Decreased renal filtration and plasma flow with retention of sodium occurs in congestive failure when the cardiac output is decreased. Catheterization of the heart has added essential information on pressure changes during exercise, and made possible a new theory proposed by Landis, to explain the fundamental defect in congestive heart failure. This involves numerous transitory elevations of venous pressure in the right heart as the result of injudicious exercise, that is, muscular activity in a cardiac patient with reduced competence. Pooling of blood in the venous bed then occurs, reducing the effective cardiac output. Reduction in glomerular filtration follows and sodium is retained, then plasma proteins and erythrocytes increase and a plethora develops. The added circulatory volume is temporarily of benefit to the active cardiac patient while up and about, but dangerous at night when the patient lies down. Persistent elevation of the peripheral venous pressure is the ultimate end result of chronic congestive failure. This theory satisfactorily explains the occurrence of cardiac œdema on the basis of locally increased venous pressure and the retention of sodium. Cardiac failure is no longer considered forward or backward failure but a combination of both. Treatment is adequate rest, medication to increase cardiac output, that is digitalis, the restriction of sodium and diuretics.

Dr. W. R. Campbell, speaking on Renal Œdema, said that, in acute glomerular nephritis, the endothelium of some capillaries was more permeable than others resulting in so-called "universal œdema". This is associated with vaso-motor instability, the lungs may fill up, venous pressure is high. There is no change in blood electrolytes. These patients have an opaque pallor and appear stupid. The treatment is restriction of salt and water. Digitalis should be given if the heart is failing. Diuretics never should be given. Magnesium sulphate should be given in small doses. If the nephritis does not heal, a lower concentration of plasma albumen occurs. Loss of plasma albumen is worse than loss of globulin. If the serum albumen is half its normal percentage œdema cannot be controlled. Give less than 150 grams protein in daily diet. Give 50 grams of urea a day but administration of concentrated serum albumen may be more effective. Diuretics have a temporary favourable effect but result in ultimate disaster.

He said that, in chronic nephritis, the plasma albumen is deficient. In these cases, diuretics should be used with caution; as time goes on, these kidneys become more impermeable. Salt is excreted well. The final result is anæmia leading to intractable anoxia.

Dr. R. B. Kerr, speaking on œdema associated with Nutritional and Hepatic Disorders, said that, with undernutrition, is associated bradycardia and low blood pressure. Some cases have low serum protein probably due to low protein intake. When serum protein is less than 4.5 to 5.9 mgm. % œdema results.

Hypoproteinæmia predisposes to œdema but salt and water are needed to produce it. Hypoproteinæmia occurs

in (1) starvation; (2) gastrointestinal tract disease; (3) burns with pus, after hæmorrhage; (4) diminished formation of protein by the liver. The treatment is ingestion of milk, eggs and meat, also plasma transfusion.

In thiamin deficiency resulting in wet beri-beri, the venous pressure is raised, with large heart and tachycardia. There were three types of œdema seen in Hong Kong prisoners. First, that resulting from thiamin deficiency; second, a persistent type not responding to thiamin; third a kind that came on after release.

Since the liver is the source of fibrinogen, long standing liver disease can effect plasma protein. In acute infections, hepatic œdema occurs in lower extremities, in abdominal wall, but rarely in the face. The serum protein may be low or normal. The albumen fraction is less and the globulin fraction is raised. The low serum albumen is due to low manufacture and loss in ascitic fluid. Daily loss of protein in ascitic fluid can be 18 grams of protein.

The treatment of œdema due to liver disease is to feed high protein diet with added vitamin B.

LILLIAN A. CHASE

La Société de Chirurgie de Montréal

La société de chirurgie de Montréal 12 fevrier, 1947.

LES RISQUES OPÉRATOIRES CHEZ LES CARDIAQUES: COMMENT LES EVALUER ET LES DIMINUER. — Mercier Fauteux.

Dès le début de sa communication, le docteur Mercier Fauteux délimite le cadre de son sujet. Les cardiaques qui viennent pour une opération d'urgence ne seront pas considérés; il en est de même des cardiaques avec insuffisance du cœur avérée et, par conséquent, aisément reconnue cliniquement. Ce sont ceux chez qui l'examen subjectif et objectif ne révèle pas d'insuffisance du myocarde ou d'insuffisance coronarienne dont il sera question.

Comment évaluer chez ceux-ci la valeur fonctionnelle du cœur?

Depuis environ six ans, le docteur Fauteux a mis au point un ensemble d'examens pré-opératoires pour tous les malades qui doivent être opérés sur le cœur. Sans vouloir prédentre que cette série d'examens puisse donner des résultats entièrement précis, il juge qu'ils peuvent aider considérablement dans le dépistage de l'insuffisance cardiaque ou coronarienne latente. Il énumère cette série d'examens et discute leurs avantages respectifs. Ce sont: (*a*) l'examen radiologique du cœur et de l'aorte, (*b*) la capacité vitale, (*c*) la prise quotidienne de la pression artérielle, et (*d*) des tests de tolérance à l'exercice. Ces derniers, qui sont faits d'une façon très élaborée, sont minutieusement décrits par le rapporteur.

Comme tous les cardiaques sont exposés aux complications de thrombose post-opératoire, le docteur Fauteux insiste sur l'importance de l'étude du temps de coagulation et du "prothrombin time" avant d'entreprendre une intervention. Au sujet de la thérapeutique préventive des accidents de thrombose, il rappelle brièvement la valeur respective du dicoumarol et des ligatures veineuses, et note que le mérite respectif de ces deux méthodes est loin d'être encore exactement fixé.

Le rapporteur termine son exposé en discutant la valeur de la digitale et de la quinidine comme médication pré-opératoire. Il ne juge pas qu'il soit nécessaire de digitaliser systématiquement tous les malades. La digitale a des indications bien précises. Tant qu'à la quinidine administrée dans le but de diminuer l'irritabilité cardiaque ou encore de contrôler certaines tachycardies ventriculaires, il considère que son administration est peut-être plus dangereuse qu'utile lorsque le médicament est employé a des doses réellement actives.

La société médicale des hôpitaux universitaires de Québec

Société médicale des hôpitaux universitaires de Québec le 20 décembre, 1946.

LUPUS TUBERCULEUX.—E. Gaumond et J. Grandbois.

Les auteurs après avoir rappelé à quelles mutilations aboutit parfois le lupus tuberculeux, rapportent l'observation de deux malades atteints de cette dermatose, l'un depuis quinze ans, l'autre depuis trente ans. Ils ont utilisé la technique de Charpy qui consiste à donner de la vitamine D2 à raison de 15 milligrammes à la dose, trois fois la première semaine, deux fois par semaine pour les trois semaines suivantes et une fois par semaine par la suite jusqu'à guérison du lupus. Les résultats constatés dans ce rapport préliminaire sont des plus prometteurs.

La technique mérite d'être étudiée davantage tant à cause de son intérêt dans le traitement des tuberculoses cutanées que dans la possibilité de son action curative dans d'autres formes de la tuberculose.

LA VALEUR DE LA GASTROSCOPIE.—Jean-Paul Dugal.

L'analyse de 600 dossiers de malades ayant subi un examen gastroscopique permet de tirer les conclusions suivantes: La gastroscopie est un procédé d'examen qui complète une étude de l'estomac faite préalablement par les rayons X. Le gastroscope décèle des cancers qui ont échappé à l'œil du radiologiste et est surtout utile pour contrôler certaines images fortement suggestives de néoplasme. Cette exploration sert à résoudre les nombreux problèmes que posent les différentes variétés de gastrite. 21% des malades examinés présentaient des signes endoscopiques de gastrite. La méthode prouve aussi son utilité dans l'étude de l'ulcère.

Quelques observations et radiographies sont présentées.

AUTOPLASTIES ET GREFFES CUTANÉES.—Jacques Turcot.

Voici une mise en lumière des méthodes classiques de pratiquer les autoplasties et les greffes cutanées. D'abord les autoplasties à lambeaux suivant les méthodes française, indienne et italienne qui sont décrites et illustrées par des cas concrete avec photographies. Puis, on revoit les méthodes de greffe de peau libre; soit greffes en ilots, selon Réverdin et Davis; soit greffes dermo-épidemiques minces d'Ollier-Thiersch ou greffes dermo-épidemiques épaisses de Blair et Brown; et finalement les greffes de peau totale de Wolf-Krause.

Les indications des différentes méthodes sont discutées et l'on voit en fin de compte que le dermatome de Padgett a résolu presque tous les problèmes du choix de la méthode. Quelques cas sont encore présentés avec photographies. Puis l'on discute du moment at de la méthode de greffe chez les brulés. Enfin suivent des considérations sur les facteurs de prise et les facteurs de succès esthétique.

UN CAS D'HÉMOPHILIE.—Robert Caouette.

C'est l'observation d'un hémophile qui, pour la seconde fois, a vu la mort de près à la suite d'extraction dentaire. On peut retracer par l'étude généalogique que la diathèse hémophilique remonte du côté maternel de la mère de notre hémophile. La littérature médicale révèle que la cause de cette tare est encore obscure et que la thérapeutique est encore décevante. Pour le moment, les transfusions de sang et de plasma demeurent encore l'arme d'attaque de choix.

LA RACHIANESTHÉSIA, PROCÉDÉ THÉRAPEUTIQUE ET DIAGNOSTIQUE.—L.-Emile Bélanger.

La rachianesthésie a été appréciée à certaines périodes. En d'autres temps, elle fut l'objet de critiques très sévères à cause des accidents et des séquelles nerveuses qui suivirent son emploi. De nos jours, ce mode d'anesthésie est d'acceptation plus facile dans les

centres médicaux, grâce à l'usage du pentothal, de l'oxygénothérapie et de la respiration artificielle sous pression positive. De plus l'administration de la drogue par un anesthésiste spécialisé diminue de beaucoup ces incidents. Dans ce travail, la rachianesthésie est proposée comme procédé thérapeutique dans le traitement de l'œdème pulmonaire, la crise d'hyperthyroïde et l'anurie réflexe. En second lieu, il y aurait avantage à se servir de ce procédé diagnostique pour reconnaître la qualité des troubles circulatoires des membres inférieurs, l'origine des douleurs "fantômes", la valeur curative de la sympathectomie lombaire dans le traitement du magacolon et de l'hypertension artérielle.

En conclusion, il s'agit d'une théorie nouvelle susceptible d'indications très utiles dans l'avenir.

Vendredi, le 7 février 1947.

PTERYGIUM COLLI CHEZ UN GARÇON, AVEC SYNDROMES DE TURNER ET DE KLIPPEL-FEIL ASSOCIES.—C. A. Martin.

La palmure de cou se rencontre dans deux affections congénitales: le syndrome d'infantilisme pterygonuchal de Turner et le syndrome de réduction numérique des vertèbres cervicales de Klippel-Feil. Après une revue de l'historique de la question et de l'exposé de la symptomatologie des deux malades, on fournit l'observation d'un garçon de 18 ans qui présente l'association des deux syndromes.

SYNDROME D'HYPEROSTOSE FRONTALE INTERNE.—Mathieu Samson.

Le syndrome d'hyperostose frontale interne a fait en ces dernières années l'objet de nombreux travaux, qui, tout en attirant l'attention des milieux spécialisés, n'a pas semblé intéresser le grand public médical.

On admet que l'hyperostose est relativement fréquente et qu'elle doit se rencontrer dans la proportion de 1 à 2% de tous les malades admis dans les hôpitaux généraux. Si elle n'est pas mentionnée plus souvent dans les rapports médicaux, cela tient, le plus souvent, à ce que le clinicien n'y porte pas attention; on interprète, comme une anomalie morphologique banale, l'épaississment, des os du crâne, qui est une manifestation locale d'un trouble du métabolisme général. C'est ainsi que, dans notre milieu, à mesure que l'attention de nos cliniciens est attirée vers ce syndrome, nous voyons le nombre de nos cas augmenter. En 1946, par exemple, nous en avons trouvé plus de vingt cas.

Le syndrome comporte d'une part un épaississement des os de la voûte du crâne, et, d'autre part, des symptômes à la fois psychiques et physiques, tels que: céphalée, obésité type rhizomélique, sensation de fatigue, ralentissement psychique peut aller jusqu'à la démence, etc.

PSYCHOSES ALCOOLIQUES À L'HÔPITAL SAINT-MICHEL-ARCHANGE DEPUIS CINQ ANS.—A. Pelletier et G.-H. Larue.

Des 4,992 patients admis à l'hôpital du 1er janvier 1942 au 31 décembre 1946, seulement 35 eurent un premier diagnostic de psychopathie alcoolique, soit un pourcentage de 0.70 de 1%. Par la suite, plusieurs de ces diagnostics furent revisés. Il s'agissait de formes de maladies mentales telles que: Manie aigue ou chronique, de psychopathie constitutionnelle, de paranoia et de démence prococe, de délire, accompagnées d'intoxications alcooliques aigues ou simplement d'alcoolisme.

Il découle de ces observations que les cas de psychoses alcooliques sont très râres à l'Hôpital. Les alcooliques que nous voyons et qui sont amenés comme tels, présentent en réalité, pour la plupart, des maladies mentales dont l'alcoolisme est un épiphénomène.

Nous considérons la plupart des alcooliques comme des malades. Et nous croyons que pour faire une lutte plus efficace au fléau de l'alcoolisme nous devons nous attaquer non pas à l'alcool, mais à l'individu, à l'alcoolique qu'il faut aider, soutenir, encourager et traiter.

MISCELLANY

UNRRA Health Division Closes

The UNRRA Health Division, the largest international health organization the world has yet known, will wind up its activities on March 31, 1947, after more than three years of work. During this time UNRRA has made available to the health departments of 13 liberated countries the advice and assistance of its international health staff, and has also given medical and sanitation services to over a million men, women and children in the camps for displaced persons in the Middle East, Germany, Austria and Italy. To make this work possible it was necessary to recruit from 35 countries a staff totalling nearly 1,200 professional persons, including doctors, nurses, sanitary engineers, epidemiologists, nutritionists, and experts in medical supplies and hospital equipment.

Dr. Wilbur A. Sawyer, Director of UNRRA's Health Division, who was formerly Director of the International Health Division of the Rockefeller Foundation, feels that the results of UNRRA's health work have exceeded all expectations. Europe has gone through the first year and a half after the most widespread and devastating war in history with no major epidemics, which is a much better record than was made after the last war, and this in spite of population displacements many times as great.

For several months now, the Health Division has been handing over phases of its activities to the Interim Commission of the World Health Organization. The administration of the international sanitary conventions of 1944 was transferred on December 1. A number of UNRRA health functions in European countries and Ethiopia, including malaria and tuberculosis control and the training of health personnel through fellowships and teaching, were turned over to the Interim Commission on December 31. Likewise, the Health Division's activities in relation to displaced persons in Europe and the Middle East were transferred to the UNRRA Displaced Persons Division, an arrangement which should continue until the International Refugee Organization of United Nations takes over the whole displaced persons program. The China health program will be transferred on March 31.

In order to make it possible for the Interim Commission to carry on some of UNRRA's health work pending the full establishment of the World Health Organization, UNRRA has authorized the transfer of one and one-half million dollars to the Commission.

CORRESPONDENCE

Well, What Do You Know? I'm a Psychiatrist and didn't Know it.

To the Editor:

One can imagine the above monologue being echoed by scores of members of the profession after reading the article, "Psychiatric Objectives", by R. R. Grinker, in the February number of the *Journal*. For twenty-five years one heard much about the split personality of man. For five years one heard much about the split between personality and material man. Now it would appear that by healing the split between personality and man, one may succeed in healing the split personality of man.

Nature tends to repeat and to simulate phenomena. Man tends to rediscover them. Time was when man was recognized to be sick in body and soul. The one who recognized this phenomenon, and tried to do something about it, became known as a physician. Then followed the age of splitting. In due course disease of body became split off from disease of soul. Still later

disease became split into disease of the various departments of the body and of the various departments of the soul. Investigators strove unceasingly to multiply the splittings, and educators strove unceasingly to split the physician in a frantic effort to keep pace with the splittings of the investigators. The race was on; action and reaction; nature repeating itself, paralleling the myriad of similar conflicts of natural enemies. As disease became highly departmentalized by fission, the physician became a galaxy of specialists, with some gains and some losses on both sides.

The victim of disease gained the products of research and technical skill, and lost the benefits of psychiatry, practised consciously or unconsciously, by the patriarchal physician, and later the family doctor. The physician gained in scientific knowledge and technical skill, and lost in psychiatric approach and magnetic power. This was inevitable as the student of medicine became harassed by an overwhelming volume of facts and formulæ to be absorbed and assimilated in one short span of life, being ever shortened by the frantic race to keep pace with the contest.

Have the investigators and the educators not progressed or regressed, too far? Or is nature, as is its habit, about to complete a cycle, and bring the opposing forces back to where they started? Such a revolution might bring once more the man sick in body and soul, ministered to by a whole physician. The sick man might benefit, and the physician might find time to get acquainted with his own family.

H. H. HEPBURN, M.D.
(A split physician)

Edmonton, Alberta.

SPECIAL CORRESPONDENCE

The London Letter

(*From our special correspondent*)

COMPROMISE

As was generally expected, the special delegate meeting of the British Medical Association accepted their Council's resolution that the Association should enter into negotiation with the Minister of Health "provided that such discussions are comprehensive in their scope and that the possibility that they may lead to further legislation is not excluded". Acting in the same conciliatory spirit the Minister agreed to resume discussions "in the light of this resolution" and has asked the negotiating committee of the Association to meet him in regard to the administration of the Act. This invitation in turn has been accepted by the Committee, so that the field is now set for the final stage of what has proved to be one of the most controversial incidents in the long history of the medical profession in this country.

Meanwhile the Minister has set up a committee to consider the remuneration of specialists and consultants in a publicly organized service. The chairman of the committee is to be Sir William Spens who has already presided over the committee that reported on the remuneration of general practitioners in such a service.

THE NURSING PROBLEM

Among the many shortages of "man-power" none is so tragic in its consequences as that of nurses. All over the country hospital wards are having to be closed because of shortage of nursing staff, accentuated not infrequently by shortage of domestic staff. Hospital authorities throughout the country are now paying serious attention to a plan which has gone far towards solving the problem in Gloucestershire. This consists of the employment of part-time nurses. The essentials of the scheme are that these part-time nurses work a four-hour shift; they are accepted as part of the staff and not as mere "auxiliaries", they are given reasonable pay and transport to facilitate their getting to their respective hospital.

Preliminary fears that this arrangement might upset the permanent staff have proved unfounded, very largely because it has allowed of the permanent staff having shorter hours of work and regular times off duty. The scheme has now been taken up by the Minister of Health for Greater London, and an appeal has been made for volunteers. To date a total of over 850 volunteers have responded to the appeal. Whether the scheme will prove as effective in hospitals dealing with acute cases as it has in those housing the chronic sick remains to be seen, but there is little doubt that, handled in the right spirit, it will go far towards helping to solve a problem that was beginning to interfere seriously with the health services of the country.

A further sign of the careful thought that is being given to this problem is the decision of the Council of the Royal College of Nursing to set up a school of nursing which it hopes will be incorporated into the University of London. Schools of this type are well established in Canada, but the Universities over here have been slow to open their doors to the technical professions, and it is not yet clear what the response of the University authorities to this suggestion will be. There is a school of thought over here that contends that the nurse's training is already too academic, and that what is required is a return to a more practical training.

THE KING'S FUND

This year marks the jubilee of the King Edward's Hospital Fund for London. The Fund was the outcome of a suggestion of King Edward VII, then Prince of Wales, that such a fund would be the most appropriate National Memorial on the occasion of the Diamond Jubilee of Queen Victoria. The aim of the Fund was to assist the voluntary hospitals of London to maintain an adequate service to the community and at the same time to provide "the means of medical education and the advancement of medical science". Since those days it has gone from strength to strength, and in 1945 its income was practically £500,000. But it has never been merely a money-raising organization. Indiscriminate subsidies to hospitals have never been its policy. No hospital has received a grant from the Fund unless it attained to a certain standard of efficiency, and the Fund has been largely responsible for introducing a unified system of accountancy for the London hospitals.

Another example of its efficient service is the report on hospital diets which it published a few years ago. This report has done more to ensure an adequate dietetic standard in our hospitals than any other measure that has been considered. Indeed, the standing of the Fund is such that hospitals will accept suggestions from it that they would never dream of even considering were they to come from any other source. An excellent example of our traditional gift for producing reforms by voluntary effort, it has served the citizens of London well for the last fifty years. There are many who believe that in the years to come it will serve an equally useful function by bringing a leavening of voluntary service to the austere regimen of a "publicly organized service".

LORD BEVERIDGE AGAIN

The same vitality of the voluntary spirit is well exemplified in the announcement that Lord Beveridge "has started work on a third report based on the last of the three principles he laid down in his report on Social Insurance and Allied Services, that 'social security must be achieved by co-operation between the State and the individual'." While the inquiry will cover the whole field of voluntary social service, the emphasis will probably be upon the rôle of friendly societies, building societies and housing associations. Much of the field of social service has already been covered by the surveys of the Nuffield Foundation, and by linking up this work with that of these other voluntary organizations, the survey will subserve a most useful function. Carrying as it will the signa-

ture of the greatest living authority on the social services of the country, the report will be looked forward to with the keenest of interest by all who are concerned with the future welfare of the citizens of these Islands.

WILLIAM A. R. THOMSON

London, March, 1947.

ABSTRACTS FROM CURRENT LITERATURE

Medicine

Gastragogue Effect of Laxatives and Allyl-Bromide Mixture. Feinblatt, H. M. and Ferguson, E. A., Jr.: *Am. J. Digest. Dis.*, **13**: 386, 1946.

Defining a gastragogue as a substance that aids in emptying the stomach of its contents, Feinblatt and Ferguson reported their clinical and roentgenographic study of the allyl-bromide mixture consisting of all the natural products of bromination of garlic. The allyl-bromide mixture was demonstrated to be a useful agent in stimulating gastric motility and physiological emptying of the stomach which shows retention. The gastragogue effect was associated with subjective relief of symptoms. When allium sativum is brominated, the resulting allyl-bromide mixture shows the clinical action of a carminative. Gastric analyses on rats showed definite evidence of gastric stimulation. The laxative drugs studied did not increase stomach motility or secretion.

Malnutrition in Released Prisoners-of-War and Internees at Singapore. Mitchell, J. B. and Black, J. A.: *The Lancet*, **251**: 855, 1946.

The authors attempt the difficult task of summarizing the medical histories of a series of 1,230 prisoners-of-war who were admitted to the 47th British General Hospital, Singapore. Attention is concentrated on 577 patients who were admitted primarily for malnutritional disorders. The patients had been subjected to a diet usually deficient in proteins, fats, and vitamins, for a period, in most instances, of three and a half years. Highly polished rice had been the staple article of food. The daily diet may have contained an average of 2,000 to 2,500 calories; precise figures were not obtained. Of the patients admitted because of malnutrition, neurological changes were present in 26.3%; tongue lesions, in 19.1% amblyopia, in 6.2%; skin lesions, in 4.3%; signs of riboflavin deficiency, in 0.5%; and other lesions, in 43.5%. Sixty-one per cent were œdematous and 23.1% had specific or non-specific diarrhœa. Many combinations of signs of food deficiency were seen in single individuals.

In the most severely affected individuals, lethargy and complete lack of interest in the patient's surroundings were conspicuous. The neurological signs and symptoms were predominantly those of peripheral neuritis and included paresthesias, weakness, sometimes coming on suddenly, absent or diminished tendon jerks, and areas of anæsthesia and dissociated sensory loss. Loss of joint sense and some ataxia were common. The muscular weakness developed most commonly and most severely in the leg and forearm muscles. The tongues, when affected, were sore and red, pale and atrophic, red and atrophic, or magenta coloured. Hyperkeratosis, often in association with diarrhœa and sore tongue, was the commonest skin lesion seen. In the most poorly nourished, however, the skin was often thin, dry, and scaly. Unexplained petechial rashes and ecchymoses appeared in some patients without relation to the severity of malnutrition as judged by other criteria. Unexplained tachycardia, which did not respond to thiamine treatment, occurred in 58 of the 577 patients. Sudden collapse into a shock-like state and congestive heart failure were observed, but, apparently, less frequently. Thiamine in one case, and thiamine and digoxin in another quickly relieved two patients with congestive failure. In most cases of œdema its pathogenesis was not explained. Its presence and degree were not related to the level of the plasma proteins. It often became worse during the first few days of treatment.

Treatment, in general, consisted of a graded diet, vitamin supplements when their use seemed indicated, and nursing care. During the early days of treatment diarrhœa was sometimes very troublesome. It often responded to a temporary reduction in diet. Reconstituted plasma was given intravenously to a few patients with persistent œdema. On two occasions, fatal pulmonary œdema followed its use. It is interesting that occasionally the signs of riboflavin deficiency became worse or appeared for the first time after treatment was instituted. Death attributed in whole or in part to malnutrition occurred in 18 cases.

W. L. LOCKE

Agranulocytosis Caused by Thiouracil. Morton, J. H.: *Am. J. Med.*, **2**: 53, 1947.

This article reviews 61 cases of agranulocytosis occurring in patients having hyperthyroidism treated with thiouracil. Only those cases are included in which the leukopenia was extreme, the granulocytes were absent or markedly reduced in numbers, and in which there were clinical manifestations caused by the reduction in the number of circulating leucocytes. The incidence of agranulocytosis, so defined, in patients treated with thiouracil averaged about 1.8%. The mortality rate was 28%. In 85% of cases the symptoms appeared between the third and the twelfth week of therapy but, in some instances, symptoms appeared as early as one or two weeks and as late as 52 weeks after the commencement of treatment. Emphasis is laid on the necessity for constant vigilance, particularly during the danger period just indicated, to detect the first signs of incipient agranulocytosis. Any untoward change in the white cell count (even a moderate unexplained leucocytosis) should call for added caution. The patient should be instructed to discontinue the drug and report to his physician should there appear the slightest evidence of toxicity, such as the mildest sore throat, malaise, or a rise in temperature. After discontinuance of the drug, penicillin (500,000 units daily) is the most effective therapeutic agent. Supplementary treatment with whole blood and pyridoxine is recommended. The sulfonamides should not be used if penicillin is available. The author emphasizes that vigorous treatment should begin as soon as the agranulocytosis is detected. To withhold treatment because the patient is asymptomatic at the time may end in disaster.

W. L. LOCKE

Treatment of Ulcerative Colitis with Thiouracil. Martin, L.: *The Lancet*, p. 944, 1946.

Since so little is known about the cause of this disease, the author feels justified in testing any remedy that is not liable to be toxic. Accordingly he feels that he should report four cases which showed great improvement under the administration of thiouracil.

All were women, their ages 37, 54, 20 and 26 years. Beginning with 0.6 gm. daily it was always possible to reduce the dose to 0.4 gm. and even to 0.1 gm.

These patients improved rapidly, usually being relieved of their diarrhœa and its accompanying discharge within eight or nine days. In addition to this, examination of the sigmoid mucous membrane revealed great improvement. Some relapses occurred which responded to an increase in the dose or renewal of discontinued treatment.

The author is aware that this treatment is in its infancy but hopes that others will endeavour to find out what the possibilities of this treatment are.

P. M. MACDONNELL

Surgery

Chlorophyll in Wound Healing and Suppurative Disease. Bowers, W. F.: *Am. J. Surg.*, **73:** 37, 1947.

In recording observations of the use of water-soluble derivatives of chlorophyll in 400 clinical cases, the author states that this substance is effective chiefly because of its stimulating effect on tissue cells, rather than its bacteriostatic properties. Firm and rapid formation of granulation tissue is gross evidence of this, as is its drying effect in abscesses, sinus tracts, osteomyelitis and in the nose in coryza and eye infections. Its deodorizing effect in chronic osteomyelitis is marked. Chlorophyll plus penicillin is being used, but only recently, so that evaluation is incomplete.

Experience with the use of chlorophyll in pilonidal cyst wounds, fistula-in-ano wounds, sloughing tumours, empyema, wound sinus tracts, perineal wounds after abdominal-perineal resection, burn and other plastic cases, bed sores, eye infections, compound fractures, ear, nose and throat infections, renal infections and now specific urethritis was almost uniformly satisfactory. Epithelialization as well as granulation is stimulated. No skin irritation or adverse systemic reactions were encountered and most patients found it a more comfortable topical application or irrigant than other solutions. In all suppurating cases, pus formation ceased in two or three days. The rapid relief of nasal obstruction could only be explained by quick resumption of ciliary movement. Chlorophyll is very bland even when instilled into the eye or pleura. BURNS PLEWES

The Excretion and Concentration of Penicillin and Streptomycin in the Abnormal Human Biliary Tract. Zaslow, J., Counseller, V. S. and Heilman, F. R.: *Surg., Gyn. & Obst.*, **84:** 140, 1947.

Studies were carried out on 23 patients who had undergone choledochostomy and the insertion of a T tube in the common duct. Single intramuscular doses of penicillin or streptomycin were given at three days and again in three weeks after operation and bile from the T tubes were tested for antibiotic activity. Estimations of the antibiotic levels in the blood stream, liver function tests as well as the surgical pathology at operation were also evaluated.

In normal patients both streptomycin and penicillin were excreted in high concentrations in the hepatic bile. A lower concentration than 0.5 units per c.c. after 15,000 units of penicillin, or less than 1.5 units per c.c. after 100,000 units of streptomycin suggest impairment of hepatic secretion. The liver appears to concentrate penicillin, but not streptomycin. In the presence of long-persistent obstructive jaundice no antibiotic agent is secreted in the bile. These agents will probably not be useful in the treatment of acute or chronic obstructive jaundice, and it will continne to be necessary to first remove the etiological mechanical factor in such cases. BURNS PLEWES

Un diagnostic rare de péritonite par perforation. *Bull. et Mém. de la Soc. des Chir. de Paris*, **36:** 102, 1946.

Cette observation rapportée à la Soc. des Chir. de Paris relate l'histoire d'un malade gastrectomisé par l'auteur en 1937 pour un ulcère perforé et bouché de la petite courbure. L'évolution reste longtemps normale lorsqu'en 1945, à la suite de douleurs gastriques ayant persisté une quinzaine de jours, le malade présente une douleur en coup de poignard localisée à l'épigastre avec quelques vomissements bilieux. La persistence des douleurs gastriques atroces avec les signes usuels d'une perforation incitent l'auteur à poser ce diagnostic préopératoire, mais il y manque cependant les symptomes de diffusion péritonéale et l'absence de gaz pré-hépatiques.

En présence d'une sédation rapide et notable des symptomes, l'opération est différée. Mais 26 heures après l'apparition de la douleur en coup de poignard, le malade meurt. L'autopsie ne révèle aucune trace d'ulcus peptique, mais une infection du myocarde avec rupture du cœur: "forme cardio-gastro-angineuse d'infection du monocarde de Lian et Pollett, caractérisé par une douleur épigastrique ou abdominale d'apparition soudaine et d'emblée à son accès, avec ou sans irradiation ascendante, s'exagérant parfois à la pression et s'accompagnant de défense musculaire épigastrique, de vomissements, de faciès péritonéal;" affection très rare et difficile à diagnostiquer d'avec la colique hépatique ou d'avec les grands syndromes chirurgicaux de l'abdomen.

L'auteur termine son observation en préconisant l'idée que la surveillance d'heure en heure peut aider à préciser le diagnostic et à éviter ainsi une intervention d'urgence nécessairement fatale dans le cas d'infection du myocarde susceptible de guérison spontanée.

J. Leuret (en discussion) fait remarquer: "que les ulcères peptiques qui se traduisent par des symptomes cliniques ne sont généralement pas méconnus, et que ce sont au contraire, ceux qui évoluent silencieusement, non diagnostiqués et non traités qui risquent le plus de se perforer en péritoine libre."

PIERRE SMITH

Plastic Surgery

Surgical Substitutions for Losses of the External Ear. Brown, J. B., Cannon, B., Lischer, C., Davis, W. B. and Moore, A.: *Surg., Gyn. & Obst.*, **84:** 192, 1947.

Losses of the external ear often complicate other serious defects so that rapid and simple restoration is important without the use of massive, distant flaps or great numbers of operations. A fundamental plan is outlined utilizing remnants of the ear and utilizing the skin of the scalp behind it. This is attached to the denuded remnant of the ear and subsequently, a carefully modelled support is fashioned from fresh or preserved cartilage and is buried beneath the portion of post-auricular skin to be utilized as the external surface of the reformed ear. After an appropriate time, the skin flap and attached cartilage are elevated from behind forward taking care to leave a soft tissue covering behind the cartilage; the resultant bare areas on the back of the new ear and on the head are covered with a thick split graft.

Where there is insufficient skin behind the ear, or where there is not enough skin free of hair, the first step is to prepare such a suitable area by skin graft; this necessitates that subsequent stages be delayed longer. Prosthetic ears are generally unsatisfactory. Even an ear which lacks the normal minute contour is acceptable if it supplies bulk and the gross form of the normal ear. The above method requires only two or three stages. It must be modified to the need of the individual patient. L. T. BARCLAY

Obstetrics and Gynæcology

Endocrines in Gynæcology. Bourne, A.: *Brit. M. J.*, **1:** 80, 1947.

The difficulties and disappointments of endocrine therapy are emphasized. Few conditions can with certainty be cured. The obvious lesson is that we have plunged too quickly and with too high hopes from the endocrinology of animals to its application in clinical medicine. There are many difficulties in the way of clinical research, but it is badly needed. One of the chief obstacles is the complexity of biochemical assays whereby blood and urine levels of the endocrine secretions and their by-products can be measured accurately. A further field is the quantitative effect of emotional states on pituitary secretions and the rôle of the receptors of the hormones. The synthesis of stilbœstrol is an indication of what great progress would follow the synthesis of other hormones. Finally, except in the case of the "trace element" iodine and the thyroid, the relation of nutrition and other "trace elements", the ultimate source of all our secretions, to endocrine activity has yet been scarcely touched. ROSS MITCHELL

Thrombophlebitis and Phlebothrombosis in Gynæcologic Patients. Meigs, J. V. and Ingersoll, F. M.: *Am. J. Obst. & Gyn.*, **52:** 938, 1946.

All the surgeons of the Massachusetts General Hospital are convinced that interruption of the femoral veins is essential after a sublethal embolus or infarct. Nearly all are agreed that interruption of the femoral veins is essential after the diagnosis of thrombophlebitis or phlebothrombosis has been definitely made.

The danger to the patient from interruption of veins properly done is minimal and it is apparent that the operation is a life-saving one. Morbidity and mortality are extremely small in the surgical attack upon thrombosis in the veins of the legs.

ROSS MITCHELL

The Office Study of Infertility. Procter, I. M. and Dickinson, K.: *Am. J. Obst. & Gyn.*, **53:** 65, 1947.

One of each four women who complain of infertility will succeed in producing a normal, viable offspring under the treatment employed by the authors. The longer a woman accepts her infertility without treatment, the less success will be had with any efforts to correct it. Cervical erosion, infection, and general disease were a surprisingly frequent finding in this group. Abnormalities of the sperm occurred in 50% of the male partners.

Tubal insufflation is of outstanding value both diagnostically and therapeutically. Endometrial biopsy is diagnostically essential, but, with the exception of thyroid the endocrines were poorly evaluated. Thyroid is a valuable drug in the treatment of infertility.

ROSS MITCHELL

Hydatidiform Mole: A Pathologico-Clinical Correlation of 200 Cases. Hertig, A. T. and Sheldon, W. H.: *Am. J. Obst. & Gyn.*, **53:** 1, 1947.

A series of 200 hydatidiform moles, gathered consecutively over a period of eleven years from 109 medical communities in the eastern half of the United States, have been examined. Follow-up data on 94.5% of all patients are available. Microscopic criteria of six groups of hydatidiform moles have been described and illustrated. These show a marked, but not an absolute correlation between the degree of apparent molar malignancy and the tendency of the patient to develop some grade of chorionic malignancy. In 73.5% of the entire series there was no subsequent development of their pathologic or clinical malignancy, as judged from the follow-up data available on 90.5% of this particular group. In 26.5% of the entire series the various grades of chorionic malignancies occurred as follows: (*a*) chorionepithelioma *in situ* 3.4%; (*b*) syncitial endometritis 4.5%; (*c*) chorionadenoma destruens 16.0%; (*d*) chorioncarcinoma 2.5%.

The prognosis of all grades of chorionic malignancy is excellent, except for the relatively uncommon, invariably fatal, chorioncarcinoma, as judged from the follow-up data available on 89% of this entire malignant group. In the first three grades of chorionic malignancy all curable, if properly treated, clinical evidence of malignancy is usually shown by continued postmolar vaginal bleeding and/or subinvolution of the uterus. A policy of clinical watchful waiting may be followed until such objective evidence of malignancy develops without increasing the danger to the patient from chorionic metastasis.

Such individualized clinical conservatism will thus save many uteri that might otherwise be needlessly sacrificed in haste merely because the patient has passed a hyatidiform mole.

ROSS MITCHELL

Orthopædics

Penetrating Wounds of the Knee Joint. Hampton, O. P.: *J. Bone & Joint Surg.*, **28:** 659, 1946.

This describes the results of experiences in the U.S. Army in the Mediterranean theatre of operations with penetrating wounds and superimposed suppurative arthritis of the knee joint.

At the time of the initial surgical treatment, the author prefers, no matter how old the wound, an arthrotomy with excision of the devitalized tissue, including area of destroyed articular cartilage, cleansing of blood clot and debris from the joint, suture of the synovial membrane and capsule, and immobilization of the leg in a hip plaster of Paris cast. At the time of reparative surgery, preferably five to ten days later, the skin should be sutured. Immobilization should be discontinued as soon as the danger of sepsis is past and the skin has healed or is healing. Active and passive mobilization should then be instituted.

This same procedure should be followed whether suppurative arthritis is present or not. Continuous drainage of fluid from the knee joint is not satisfactory as a form of treatment in suppurative arthritis.

Systemic and local penicillin is employed in all cases. Resection is only used in a few limited cases.

GUY H. FISK

Neurology

Histopathology of Polioencephalitis Superior (Wernicke's Disease). Bailey, F. W.: *Arch. Neurol. & Psychiat.*, **56:** 609, 1946.

This is an excellent review of the whole problem. The histopathological processes underlying polioencephalitis hæmorrhagica superior are confined to the periventricular gray matter of the mid-brain, and pons as well as the thalamus and the hypothalamus. These processes consist of focal areas of small capillary hæmorrhages and necrosis. Vascular disturbances include dilatation of the capillaries, capillary budding and perivascular hæmorrhages. There is parenchymatous degeneration consisting of loosening of the ground substance. Areas of widespread necrosis of focal necrosis, and of punctate necrosis occur. Within and near these areas there is neuronal degeneration exhibiting acute swelling and hyalinization, changes indicative of interference with the chemical processes of the tissue due to lack of oxygen or inadequate elimination of toxic metabolites.

Underlying the histopathological processes there is a deficiency of nutritional factors, the chief of which is thiamine. It has been shown that there is an interference with carbohydrate metabolism, with oxidation of pyruvic acid and that there is a decrease in the amount of oxygen supplied to the tissues. The effect of the anoxia and the toxic metabolites is to interfere with the chemistry of the cells and cause their degeneration, which results in necrosis of various degrees in the tissue of the brain stem and weakening of the walls of the capillaries with extravasation of blood.

PRESTON ROBB

The Results of Treatment of Multiple Sclerosis with Dicoumarin. Putnam, T. J., Chiavacci, L. V., Hoff, H. and Weitzen, H. G.: *Arch. Neurol. & Psychiat.*, **57:** 1, 1947.

For some years Dr. Putnam has felt that the sclerotic plaques of multiple sclerosis arise as a result of venular thrombosis. It was felt that if the clotting time of the blood could be prolonged the chances of further attacks could be decreased. For this reason dicoumarin was administered to 74 patients. For various reasons the results of treatment of only 43 were reported. The period of treatment varied from six months to four years. Before starting treatment it was made clear to the patient that the treatment conferred protection only while the drug was taken, and that it would probably have to be continued for the rest of the patient's life.

Twenty-five patients suffering from a remittent form of the disease were adequately treated without interruption for a total period of approximately 61 patient years. In this group no fresh symptoms or obvious acute outbreak of symptoms occurred. Most of the 16 patients with chronic progressive disease continued in their downward course. The treatment

of two patients was interrupted for one reason or another. These patients were free from new symptoms while taking treatment, but both had acute relapses when it was discontinued. In two patients larger doses of dicoumarin failed to produce the expected increase in prothrombin time, and relapses occurred.

It should be pointed out that this treatment should only be attempted when adequate facilities for blood studies and handling of the hæmorrhagic complications are available. PRESTON ROBB

Radiology

Treatment of Malignant Tumours of the Testis. Kelby, G. M. and Stenstrom, K. W.: *Radiology*, **48:** 1, 1947.

This series is based on 100 cases of malignant testicular tumours at the University of Minnesota. The classification of the tumours is that of E. T. Bell, namely, adult teratomas, carcinomatous mixed tumours, seminomas, and chorionepitheliomas. Of these, seminomas consisted of 56% of the total and the carcinomas in 29 of the patients. Of the seminomas 65% had metastases before beginning of irradiation and of the total number of seminomas 56% survived five years or more while only one of the carcinomas survived the five years. The latter showed metastases in 86% before irradiation.

Therapy consisted of simple orchidectomy and irradiation in 90 cases; irradiation alone in six advanced cases and Hinman's operation and irradiation in four cases. Simple orchidectomy followed by irradiation is the treatment of choice in seminomas. Carcinomatous mixed tumours should be treated by radical dissection and a teratoma by simple ochidectomy. R. C. BURR

Dysgerminoma of the Ovary. Moreton, R. D. and Desjardins, A. U.: *Am. J. Roentgenol.*, **57:** 84, 1947.

Over 300 cases of this tumour are reported in the current literature, 11 cases from the Mayo Clinic from 1905 to 1943 being reviewed in this paper. Histogenesis is discussed. The majority believe that this tumour is derived from the embryonic sexual cells as a result of some undetermined stimulus.

Histopathologically the structure is that of a Grade 4 (Broders' classification) embryonal carcinoma with lymphoid stroma. The clinical outcome apparently is determined by such factors as the presence of bilateral lesions, whether or not the capsule of the neoplasm is intact, whether or not the tumour has twisted on its pedicle and other considerations. Recently the ovarian dysgerminoma has been shown to be associated with the presence of an excess of A.P.L. substance in the urine.

These tumours are highly radiosensitive being comparable to the seminoma of the testis and also to lymphoblastoma. Except in special instances in which childbirth has to be considered, the treatment which offers the best prospect is surgical removal plus adequate postoperative therapy. Metastases are best treated by radiotherapy. It is interesting to note that while seminomas metastasize to the mediastinum and to the lungs readily, such was not found in the case of dysgerminoma. Hence, treatment over the mediastinum was not employed in this tumour. R. C. BURR

Dermatology

Leukoplakia (Leukokeratosis) of the Palate, Papular Form. Its Relation to the Use of Tobacco. Cummer, C. L.: *J. Am. M. Ass.*, **132:** 493, 1946.

This condition was first mentioned in American medical literature in 1926, but Harold Orr in reporting 7 cases in 1930 was the first to describe the histological observations. Several subsequent references reflect the writer's view that it was implicated with tobacco-smoking. It is usually discovered in routine examination, as it seldom produces subjective symptoms. The eruption appears more frequently on the hard palate although the whole palate may be involved. There is a profuse and closely-packed studding with papules, usually pin-head in size although they may attain the diameter of 5 mm., usually grayish on the hard palate but bright red on the soft palate. Cummer estimates that about 1 person in every 100 presents the condition, although in his series of 6 cases in 587 palates examined none were in women and 5 occurred in the 6th and 7th decades. The condition appears to be essentially an obstruction of the orifices of the mucous glands by keratinized epithelium, accompanied by widening of the adjacent capillary spaces and mild inflammatory reaction but with no cystic or adenomatous change. Syphilis appears to have no significant relationship, but tobacco, especially pipe-smoking, is of great etiological significance. Most cases recovered only on cessation of smoking; this or wearing a protective denture appears to be essential for cure. In none of the relatively few cases recorded by observers have malignant changes occurred. D. E. H. CLEVELAND

The Management of Bacterial Infections of the Skin. Pillsbury, D. M.: *J. Am. M. Ass.*, **132:** 693, 1946.

In the treatment of acute superficial infections, the increasingly observed incidence of sensitivity reactions to penicillin used topically indicates that this agency is less useful than has been thought. In the majority of cases of the primary acute infections topical penicillin therapy is rapidly effective. Treatment of folliculitis of the beard by this agency has been disappointing, and in the secondary infected dermatoses it is much less effective, and sensitivity to penicillin may occur in as high as 25% of cases. The reactions are usually mild and in some patients it may be possible to continue the local use of penicillin with disappearance of the sensitivity. As in sulfonamide therapy it is probable that by repeated contact with penicillin either by application or injection the epidermal sensitivity will not only increase, but dermal and vascular structures will also be sensitized resulting in reactions to subsequent parenteral administration. To lessen the risk of sensitization it is recommended that penicillin ointment should not be used longer than 5 days. A concentration of not less than 500 units per gram should be used.

Sulfonamide therapy of superficial skin infection is rarely if ever justifiable. It is also observed that sulfonamide ointments are too readily available to prevent their misuse. Local hygiene of the skin is an important consideration. Beside gentle debridement, which is essential, the use of isotonic saline, boric solution or 0.01% potassium permanganate solution is recommended. None of the agencies interfere with the efficacy of penicillin locally applied.

The author believes that parenteral use of penicillin is equal to if not superior to its topical use in superficial infections. Its expense and inconvenience (two or three daily injections in the office) are disadvantages.

Among other useful preparations mentioned are ammoniated mercury in ointment concentrations of not more than 5%. On oily skin or where there is much oozing ammoniated mercury is better used in a "shake" lotion, such as calamine lotion. Castellani's carbol-fuchsin paint is highly regarded by the author. The colour is objectionable, but the preparation is not as messy as gentian violet and it has valuable antipruritic qualities. Quinolor compound ointment is especially valuable in chronic follicular infections. D. E. H. CLEVELAND

Severe Allergic Reactions to Penicillin. Mendell, T. H. and Prose, P. H.: *Am. J. M. Sc.*, **212:** 541, 1946.

Allergic reactions to penicillin are reported with increasing frequency. In the majority of instances the reactions are minor in character. Occasionally alarming reactions of such severity are observed as to necessitate immediate discontinuance of the drug. In a series of more than 500 patients treated in the Philippines in 1945, 6 cases (0.12%) reacted to this degree, 4 cases of typical drug allergy—severe and disabling pruritus,

an erythematous rash with vesicles sometimes of considerable size, swelling of the extremities, and fever, and 2 cases of a delayed reaction simulating serum-sickness were described. In the cases of drug allergy patch-tests were positive, but passive transfer and precipitin tests were negative; this is because drug allergens not being antigens no antibodies are produced. The possibility of detecting reactors before institution of penicillin therapy was investigated. Two hundred healthy persons, 50% of whom had received penicillin on some previous occasion were tested on skin and conjunctiva to 2 commercial brands of penicillin—100 with each. The tests were negative. The same results followed parenteral administration of 50,000 units to each of these patients. It is not claimed that these tests are conclusive. While severe reactors have been shown to react positively to the patch-test, it is not practical to employ it as the delay of 24 to 48 hours necessary to develop the reaction may be dangerous. It is necessary to keep in mind the possibility of an occasional severe reaction, and to recognize its nature promptly.

D. E. H. CLEVELAND

Hygiene and Public Health

A Suggested Plan for a Preventive Medical Program in a Federal Employees' Health Service. *U.S. Public Health Reports,* **61:** 1642, 1946.

The passing of Public Law 658 by the Seventy-ninth Congress of the United States makes possible the establishment of health services for Federal employees. The Act places the administrative responsibility for the health service program in the head of the Government department or agency, including Government-owned-and-controlled corporations. Such programs may be established only after consultation with the United States Public Health Service and after consideration of its recommendations, and only in localities where there are a sufficient number of Federal employees to warrant the provision of such services. The scope of the health program is limited to (1) treatment of on-the-job-illness and dental conditions requiring emergency attention; (2) pre-employment and other examinations; (3) referral of employees to private physicians and dentists; and (4) preventive programs relating to health.

In this article the essential elements believed by the U.S. Public Health Service to be desirable for such a plan, are presented in detail. It is stressed that the pervading tone and quality of the total employees' health service should be created by the influence of high professional standards and a genuine interest in and respect for the personality of the individual employee. The recommendations are given under the following headings: type of program, personnel needs, functional organization; the health program and scope of service; the component parts of each specific phase of the health program; the appropriate quarters and facilities to be provided by the agency to enable the program to fulfill its function.

The plan which has been now formulated and presented is to be subject to modification from time to time in accordance with the evolution of preventive medicine.

MARGARET H. WILTON

Study of Absenteeism During a Five-Month Period Following Influenza "A" and "B" Vaccination. Newquist, M. N. and Page, R. C.: *Indust. Med.,* **15:** 676, 1946.

That indiscriminate influenza vaccination of employee volunteers is of no apparent value in reducing absenteeism due to common respiratory infections, is the opinion of the authors following a study conducted in New York City in January, 1946.

Mass vaccination of 665 volunteers (employees) with influenza vaccine ("A" and "B") was carried out. They were given a series of two injections of ½ c.c. each, one week apart during January. The absentee records for the following 5 months (February-June, inclusive) were analyzed and compared with those of a control group of 656 employees working in the same environment, who did not take the vaccine. A table presents a detailed analysis of the data and another the tabulated replies to a questionnaire, of persons receiving the vaccine.

The group that was vaccinated with influenza vaccine ("A" and "B") had a greater absence rate (1.14 days per employee) from all respiratory tract diseases than the control group (0.91 days per employee). From colds, grippe and non-epidemic influenza the vaccinated group lost 673 days (1.01 days per employee) while the control group lost 456 (0.69 days per employee).

The authors suggest that the volunteer group was probably prompted to take the vaccine on account of frequent respiratory infections in the past; the others were mainly persons with a relatively higher respiratory disease resistance. In the opinion of the volunteers, the vaccine was of definite value but this was not reflected in the absentee rate.

The authors consider that in view of favourable reports in the literature, it is advisable for industrial physicians to keep in close touch with public health authorities in regard to the status of epidemic influenza. They suggest that when the incidence of influenza is approaching epidemic proportions, mass vaccination with influenza vaccine should be instituted so that maximum immunity will be attained before the full impact of the epidemic occurs.

MARGARET H. WILTON

OBITUARIES

Dr. Charlemagne Baribeau, aged 47, well-known Three Rivers surgeon and physician died suddenly February 8.

He was a native of St. Geneviève de Bastiscan and was educated at the Three Rivers Seminary and Laval where he graduated in medicine in 1927.

Highly esteemed by his colleagues and all with whom he came in contact, Dr. Baribeau's health had given grounds for some anxiety ever since 1945 when he suffered a cerebral hæmorrhage. He was obliged to give up practice for many months, but resumed it recently. It is believed that overwork contributed largely to his untimely demise.

He is survived by his widow, his mother, one brother and four sisters.

Dr. Albert Deans Barnet, of Guilford, Missouri, died May 4, 1946.

He was a graduate in medicine of the University of Toronto in 1887.

Dr. Charles James Bermack died suddenly in his office in Winnipeg, on February 10, aged 51. Born in Detroit, Michigan, he lived most of his life in Winnipeg and was educated in the public schools and St. John's Technical High School. He graduated in medicine from the University of Manitoba in 1916 and began practice in 1919 in Winnipeg. With Dr. S. Easton he formed the Bermack-Easton Clinic. He was a past president of the Jewish Orphanage, first Chairman of the Children's Bureau and a past master of Mount Sinai Masonic Lodge. Sport was another of his interests. He was a physician to the Winnipeg Rugby Club and for some years a member of the Winnipeg Senior Bowling league. Besides his widow, he is survived by a son, Gordon, a medical student in the University of Manitoba.

Dr. Robert S. Broad, aged 71, prominent Edmonton specialist for the last 35 years, died at his home February 3. Born in Little Britain, Ont., he graduated from the University of Toronto and began his practice in Barrie. In 1912 he moved to Edmonton and set up his practice here as an eye, ear, nose and throat specialist. He is survived by his widow, one son and three daughters.

Dr. Thomson Bickerton Edmison died at the Toronto General Hospital on January 29.

He graduated in medicine from the University of Toronto in 1903.

He is survived by one daughter and two sons.

Dr. James Joseph Finn died on February 8, 1947, at the age of 65. He practised for almost thirty years at Dundurn, Sask. Dr. Finn was born in New York City and graduated from the University of Toronto in 1913, registering in Saskatchewan in 1915. Surviving are his widow, three sons and two daughters.

Dr. R. Franklin Forrest, aged 77, died on February 8 at the home of his daughter in Maple, Ont.

Born at Mount Albert, Dr. Forrest graduated from Jarvis Collegiate and then attended the university. In 1892, he received an M.B. degree from the University of Toronto and the same year obtained the M.D.C.M. degree from Victoria University. He spent some time in postgraduate study at Edinburgh, Scotland, and received the degrees of L.R.C.P. and L.R.C.S. from there. Later he also studied at London, England, and New York.

Dr. Forrest started practice in Uxbridge where he remained for 10 years before moving to Port Hope where he practised for 30 years before his retirement. Here he was attending surgeon to the Port Hope Hospital and served as physician at Trinity College School.

He was a member of the Masonic Order, Jockey Club and the Presbyterian Church.

Surviving are his wife and two daughters.

Dr. John Gemmell died on December 24, 1946, at Assiniboia, Sask., at the age of 66. He served the Assiniboia district for about thirty years. Born in Ontario he came west in 1901 where he settled with his family in the Tuxford district. Later he left the farm, taught school and then graduated in medicine from the University of Manitoba in 1915. Dr. Gemmell was predeceased by his wife some two years ago. He is survived by one son, Dr. John Gemmell of Winnipeg.

Dr. Wilfred Lamont Graham, well known Vancouver surgeon died suddenly on February 5. He was in his 50th year.

Born at Lobo, Ont., he attended high school in London, Ont., and was a graduate in medicine of the University of Toronto. His medical course was interrupted by the First Great War when he enlisted with the 63rd (Imperial) Naval Division and saw service as a machine-gunner.

Graduating in 1923, Dr. Graham took postgraduate work at the New York Hospital and the Royal Infirmary, Edinburgh. Four years later he started private practice in Vancouver and was a member of the staff of Vancouver General Hospital. He was also connected with Shaughnessy Veterans' Hospital.

Surviving are his widow, a sister and two brothers.

Le Dr Louis-Georges Hétu, est décédé le 29 janvier à l'âge de 62 ans. Né à Upton, comté de Bagot, le défunt avait fait ses études médicales à l'université Laval de Montréal et était diplômé des universités de Paris.

Il laisse, outre son épouse, quatre frères et deux sœurs.

Dr. William Elsworth Inksetter, died on February 27, in Hamilton General Hospital at the age of 81. He was born in Copetown and attended school there and at Dundas prior to graduating from McGill University in 1890.

Dr. Inksetter did postgraduate work at Glasgow and Edinburgh followed by a practice in the Orkney Islands, his father's birth place, for a few years. He practiced with his brother, Dr. G. G. Inksetter in Costa Rica, Central America, for 20 years.

He is survived by his widow, three sons and a sister.

Dr. Newton Wilson Kaiser, died on March 24, 1946, in Toledo, Ohio.

He graduated in medicine from the University of Western Ontario in 1919.

Dr. Murdoch Gordon MacLeod, of Whycocomagh, died at the wheel of his car which plunged over an embankment some time during the night of February 26, while he was returning from a call to Lake Camp.

Born at Neil's Harbour, Nova Scotia, forty-nine years ago, he graduated in medicine at Dalhousie University in 1919. Soon afterwards he settled at Whycocomagh where he practised until his death. In a large country practice he fulfilled the best traditions of the family doctor. Although in ill health for some time he carried on. His widow and four daughters survive.

Dr. I. W. T. McEachern, aged 75, prominent Edmonton doctor for the last 30 years, died suddenly February 6.

Although he retired from active practice about a year ago, he had still carried on as a doctor in the cancer clinic, devoting much time to this work. Born in Cumberland, Ont., he took much of his early education in the east and was a graduate of McGill University in 1903. In 1904 he came west, settling near Wetaskiwin, and at that time was the only doctor between there and Saskatoon. In 1907 he established a 20-bed hospital in Bawlf, Alta., and in 1915 went to New York for a postgraduate course.

On his return to western Canada, he established a surgical practice in Edmonton and had practised there ever since. For a number of years he was a member of the surgical staff of the University of Alberta and in 1919 was awarded a fellowship in the American College of Surgeons—one of the first four awarded in northern Alberta.

An ardent sportsman, he played lacrosse in his early days and was a member of the Edmonton Mayfair Golf Club.

He is survived by his widow, one daughter, and a sister.

Dr. Alfred Hope Macklin died on October 12 in Goderich, Ontario.

Born in 1859, he graduated in medicine from the University of Toronto in 1896.

Dr. W. Alleyne Marshall, aged 50, died on February 6 in Winnipeg General Hospital.

He was born in Carberry, Man. He was a veteran of World War I, in which he served with the British Air Force. He held the rank of Lieutenant and served with the Imperial Coastal Patrol in England. He was a member of the Wartime Pilots association.

He is survived by his widow and a sister.

Dr. Thomas MacKetchie Milroy, who practised in Winnipeg for fifty years, died at Vancouver, B.C., on January 31. Born in Galt, Ont., he graduated in medicine from Trinity University Medical Faculty, October 3, 1882, and was licensed in 1885. For some years he was a leading practitioner in Portage la Prairie, then moved to Winnipeg. He was on the staff of Manitoba Medical College and for many years he served with the late Dr. H. H. Chown as medical examiner for the Great West Life Assurance Company. He took an active interest in the Canadian National Institute for the Blind. He was Consultant Emeritus on the honorary attending staff of the Winnipeg General Hospital.

Dr. Frederick James O'Connor, died on March 29, 1946, in Syracuse, New York.

He graduated in medicine from the University of Toronto in 1909.

Dr. Joseph Edgar Overholt died in Louth Township on February 24 in his 92nd year.

He is survived by his widow and two sons.

Dr. William George Penney, aged 60, died on February 21 at his home in Toronto. Born in Toronto, he attended Boulton Ave. School and Jarvis Collegiate, graduating in medicine from the University of Toronto in 1909. Dr. Penney was an elder in Hope United Church and a past master of Mimosa Lodge, A.F. & A.M. He was also a member of the Toronto East Physicians' Association. In his earlier years he played soccer with the Thistle team and hockey with the All Saints' hockey team.

Surviving are his widow, four sons and a sister.

Dr. Herman Richard Rahner died on April 10, 1946, in Erie, Pennsylvania.

He graduated in medicine from the University of Toronto in 1923.

Dr. Herbert Leo Sims died unexpectedly on January 29 at his home in Ottawa.

In spite of his prominence as an ear, nose and throat specialist, many Ottawans knew him best because of the interest he took in all phases of sports. Long connected with the Ottawa Football Club, he was its president when the Rough Riders' team won the Dominion championship in 1926. He attended local separate schools, the University of Ottawa and McGill University, from which he graduated with his M.D. degree in 1906.

For the first three years following his graduation he was employed in a professional capacity with the National Transcontinental Railroad. He then undertook postgraduate training, first at New York and then at hospitals at London, England, Vienna and Berlin. In 1913 he returned to Ottawa to establish the practice which soon became one of the most extensive in Canada.

He participated actively in sports and was often described as an "all-round athlete". While attending university there he played hockey for both the Ottawa College team and Ottawa City League teams. Prominent in college athletics, he was a member of the McGill hockey team which twice won the intercollegiate championship. While studying at New York he joined the New York Athletic Club, on whose senior hockey team he played.

A keen golfer, he won many trophies in Ottawa and district. Sporting organizations to which he belonged included Rivermead Golf Club, the Ottawa Hunt Club, the Rideau Curling Club and the Gatineau Fish and Game Club.

In addition to his memberships in sportsmen's clubs, Dr. Sims was a member of several professional associations. These included the Ottawa Medico-Chirurgical Society, the Ontario Medical Association and the Canadian Medical Association. He was also a member of the University Club, the Seigniory Club and the Knights of Columbus. Of Roman Catholic faith he attended St. Theresa's church.

He is survived by his wife, three daughters and one son.

Dr. Alvie Earl Stewart, aged 53, died on February 18 at St. Joseph's Hospital, Toronto. Since his retirement in 1945, he had resided in the Kingsway.

Dr. Stewart was born at Hamilton, graduating in medicine from the University of Toronto in 1920. He interned at St. Michael's Hospital, Toronto; Mountain Sanatorium and Hamilton General Hospital. After four years' practice in Merlin, Ont., he spent two years in postgraduate study in London, Eng., Edinburgh and Berlin. Returning to Canada, he practised in Port Perry and later Oshawa before going to Mimico in 1930. He received the Fellowship of the Royal College of Surgeons, Edinburgh.

For some years a member of the Mimico Board of Education, he served two terms as chairman. He was for many years on the staff of St. Joseph's Hospital. He was a past master of Lakeshore Lodge, A.F. & A.M., and a 32nd degree Scottish Rite Mason. Past patron of Primrose Chapter, O.E.S. of Ontario, Dr. Stewart was on the executive of the Mimico Lacrosse Club. He was an elder at Wesley United Church, Mimico.

Surviving are his widow, three daughters, his father, a brother and three sisters.

Dr. Norman Grant Tufford died on August 10, 1946, in Detroit, Michigan.

He graduated in medicine from the University of Toronto in 1923.

Dr. Euston M. Vesey died on January 19 at Hanley, Sask. Dr. Vesey was 65 years old and had practised in Saskatchewan since 1908. Dr. Vesey was born at York, P.E.I., in 1882. Graduate of McGill University in 1907, he came the same year to Canora, Sask., where he practised until about 1943. Mrs. Vesey died within seven hours after Dr. Vesey. They are survived by two sons and one daughter.

Dr. Norman Clyde Wallace, aged 76, died on February 3 at his home in Guelph, Ont., following a fairly lengthy illness.

He was chairman of the local board of health many years, and gave leadership to much progress in public health work, including local inauguration of the Christmas seal campaign for anti-tuberculosis work. President of the Children's Aid Society 10 years, he also had been president of the St. Andrew's Society and of the Guelph Horticultural Society. He was well known as a Mason, and was an active member of the board of managers of St. Andrew's Presbyterian Church many years, as well as being active in the Wellington County Medical Association.

Born at Alma, he attended Guelph and Owen Sound Collegiates and graduated in medicine from University of Toronto in 1894. After postgraduate work in New York he took over the practice of his father, the late Dr. James Wallace, in Alma. This practice he sold in 1913 to the Doctors McQuibban and he was in Europe doing further post-graduate work when war broke out. Joining the Royal Army Medical Corps he served voluntarily two years at the Beachborough Park Hospital at Shorncliffe, then joined the Canadian Army Medical Corps, from which he retired in 1919 with the rank of captain (acting major).

He will be remembered by many veterans of the First World War for his service at the military hospital in what is now the Ontario Reformatory here, from 1920 until his retirement, due to ill health, in 1937.

Only survivors are his widow and a sister.

Dr. Aylmer J. Weart, aged 68, of Trochu, died on February 17 in a Calgary hospital.

Dr. Weart was born in Lansdowne, Ont., and received his high school education in Athens, Ont. He graduated from Toronto University in 1905 and came west. In 1918 he enlisted with the Canadian Army Medical Corps and went overseas. The following year he returned to Canada as officer in charge of a hospital ship and was posted to some service duty in the Colonel Belcher hospital. In 1921 he resumed private practice in Three Hills and 21 years later moved his practice to Trochu. He came to Calgary last year. He was a member of the Canadian Legion and the Masonic Order.

Surviving are his widow and two daughters.

Dr. Frank Valentine Woodbury, for many years Medical Examiner for the City of Halifax, died suddenly at his home there on February 5.

He was born at Babylon, Long Island, New York, on September 22, 1881. He attended the Halifax County Academy, and later the Halifax Medical College, from which he graduated in 1903. After two years of practice in Newfoundland he pursued postgraduate studies in Edinburgh. Returning to Halifax, he continued in practice until 1915, when he joined the Dalhousie Medical unit and went overseas. Leaving that Unit for a Field Ambulance, he was eventually promoted to the rank of Lieut. Colonel, and served as Assistant Director of Medical Services, Canadian Army Overseas until the close of War I.

Soon after his return to Canada in 1919, Dr. Woodbury became Medical Examiner for the City of Halifax and the Town of Dartmouth. He continued the general practice of medicine, however, with some emphasis on anæsthesia, and also served as United States Immigration Medical Examiner.

As an outcome of his Medical Jurisprudence, Dr. Woodbury lectured on that subject for many years at Dalhousie University. From its origin in 1908 he was active in teaching at the Dalhousie Dental School, and after 1912 was its Professor of Oral Surgery.

Dr. William Lorne Yule died on February 17, 1946, in Columbus, Ohio.

He graduated in medicine from Queen's University in 1908.

NEWS ITEMS

Alberta

The Edmonton Academy of Medicine met in the Medical Building of the University of Alberta on Wednesday February 5, 1947. Following a brief business period Dr. E. B. Quehl presented a paper on the "History of blood transfusions". Dr. W. C. MacKenzie presented a paper on "Modern management of hyperthyroidism". Excellent discussion led by Dr. J. K. Fife followed presentation of this paper. Dr. Wallace Wilson, President-elect of the Canadian Medical Association, was a guest at the meeting. Dr. Wilson extended the greetings of the Canadian Medical Association to the Edmonton Academy of Medicine and spoke briefly on the pre-paid medical plan in operation in Vancouver.

The Refresher Committee have announced the dates of their refresher course, which is to be held at the University of Alberta during the week commencing May 12, 1947. Three outside speakers have been arranged for to attend the course. Dr. F. R. Schemm, of Great Falls, Montana, will speak on medical subjects; Dr. Roscoe R. Graham, of Toronto, on surgical topics; and Dr. Edwin Robertson, professor of Obstetrics and Gynæcology of Queen's University, will represent his field.

The Committee on Program and Arrangements for the 1947 convention of the Alberta Division are busy drafting the program. It is proposed that the entire convention will consist of a series of papers dealing with recent advances in medicine and surgery. The committee consists of Dr. Harold Orr, Chairman, Drs. R. K. Thomson, W. C. MacKenzie, A. H. Maclennan and J. A. Romeyn.

In a recent questionnaire dealing with voluntary pre-paid medical care sent to the medical profession in the Province; 42.6% replies have been received, 78.9% indicating they were in favour of the presence of voluntary pre-paid medical care. There is little difference in opinion between rural and urban practitioners, between specialists and non-specialists, or between early and recent graduates.

At a special joint meeting of the Medicine Hat City Council and Hospital Board held recently, steps were taken to build a civic or a municipal hospital to replace this city's fifty-nine year old hospital.

G. E. LEARMONTH

Manitoba

On February 6, Dr. A. F. Menzies of Morden gave to the medical students a talk on Some Aspects and Problems of Rural Practice. This was the first of a series of talks to be given by rural practitioners on allied subjects, in line with a recommendation from the recent report of the Rockefeller Foundation commission. The other speakers will be Dr. A. E. McGregor, Sheridon; Dr. E. D. Bissett, Pine Falls, and Dr. J. S. Poole, M.L.A., Neepawa.

The American College of Surgeons will hold a regional meeting in the Royal Alexandra Hotel, Winnipeg, April 28 and 29. (This was erroneously shown as April 11 in the last issue of the *Journal*.) ROSS MITCHELL

A group of twelve Winnipeg physicians, all war veterans, has planned an office building at the corner of Memorial Boulevard and St. Mary's Ave., across from the Auditorium. Construction of a two-storey building faced with Tyndall stone has already begun. With three other large medical office buildings in the vicinity the area will become something of a medical centre.

Dr. Murray H. Campbell has resigned as superintendent of the Dynevor Hospital near Selkirk, Man., and has entered into practice with Dr. A. M. Campbell at 95 Sherbrook Street.

Dr. Denton Booth has been appointed superintendent of the Dynevor Hospital for Indian tuberculous patients.

On February 15, Dr. T. C. Routley, General Secretary of the Canadian Medical Association, gave an interesting talk on Recent Developments in International Medicine before the Winnipeg Medical Society.

Dr. Wallace Wilson, C.M.A. President; Dr. T. C. Routley and Dr. Kelly, Assistant C.M.A. Secretary, were present at a meeting of the local Program Committee for the coming annual meeting of the Canadian Medical Association. Their advice is most welcome. Preparations for the meeting are well in hand.

The late Dr. T. M. Milroy who died in Vancouver, B.C., January 31, left in his will $1,000 each to the Winnipeg General Hospital, the Children's Hospital and the Canadian Institute for the Blind.

B.C.G. vaccination is being carried on for negative reactors in the nursing personnel of Winnipeg and Brandon hospitals. The Sanatorium Board has recommended that the Federal Department of National Health should set up an establishment for the manufacture of B.C.G. vaccine in western Canada.

New Brunswick

Dr. Jean Webb, chief nutritionist of the Provincial Department of Health was the special speaker at the supper meeting of the Saint John Chapter of the N.B. Association of Registered Nurses at their February meeting. Dr. Webb laid emphasis on the nutrition of children of school and pre-school age.

Dr. Arthur F. Chaisson of the N.B. Department of Health speaking at the annual meeting of the Mental Hygiene Council of New Brunswick, deplored the alarming prevalence of mental diseases and the lack of proper public education concerning these conditions. He pointed out that minor mental disorders comprised a large group of disabling clinical problems sometimes masquerading under the guise of physical diseases. Their recognition and proper handling was a problem of immediate interest.

Major General R. M. Luton, Canadian observer at Bikini Atoll Bomb tests last summer was the guest speaker at the monthly meeting of the United Services Institute at the Armouries, Saint John. Many ex-members of the R.C.A.M.C. were interested listeners to the address by this distinguished Canadian service physician.

Dr. F. G. Knoll of Saint John is in Boston taking a refresher course in gynæcology.

The Saint John Board of School Trustees has asked the Provincial Department of health to make it compulsory for all children to be immunized against diphtheria before starting school. This method would insure that each child would be protected against the disease before beginning public life as distinguished from the more or less protected home surroundings.

Dr. Raleigh D. Smith has been re-elected Mayor of Saint George for the third straight term.

Dr. John A. Finley has been appointed assistant surgeon on the staff of the Saint John General Hospital to fill a vacancy on the surgical staff caused by the appointment of Dr. Geo. Skinner as a commissioner of the Hospital.

Dr. J. G. McCarrol, a graduate of Owens University, has been appointed senior intern at the Saint John General Hospital for the year 1947-48. A. S. KIRKLAND

Nova Scotia

Dr. J. C. Wickwire of Liverpool is at present attending the Harvard Graduate School of Medicine, taking a course in cardiology.

Many friends and former classmates of Dr. R. B. Archibald of Bedford Hills, New York, will regret to learn of his death. He was a graduate of Dalhousie in 1927, and a native of Centre Musquodoboit.

The strike in the coal fields of Nova Scotia and New Brunswick creates an almost complete loss of income for many physicians in these districts. Meanwhile, of course, the doctors "carry on", taking as philosophically as they may the bad times with the good.

Dr. A. B. Campbell, Chief Medical Officer of the Workmen's Compensation Board was a recent visitor to Boston.

A conference for the discussion of current problems of Public Health was held recently at the Provincial Department of Health in Halifax. Attending were the Divisional Health Officers, members of the Nursing Division, and representatives of all Departmental medical services. H. L. SCAMMELL

Ontario

Dr. A. B. Stokes of London, England has been appointed to the Chair of Psychiatry in the Faculty of Medicine, University of Toronto. Dr. Stokes is an honours graduate in the School of Natural Science at Oxford and a graduate of medicine of Oxford in 1931. He is a member of the Royal College of Physicians of London and holds the Diploma of Psychological Medicine of London. He has had postgraduate training and practical experience in the field of psychiatry in London and in Norway. During the war he was particularly interested in the rehabilitation of psychiatric war casualties. He is at present on the staff of Maudsley Hospital. Dr. Stokes, in his new post, will be responsible for undergraduate and graduate teaching of psychiatry in the Medical Faculty, and will be closely associated with the program of mental health for the province of Ontario.

The President of the Ontario Medical Association, Dr. William Magner, has announced the formation of a special committee on voluntary prepaid medical care composed of Dr. John Oille of Toronto, Dr. H. D. Logan of Lindsay, and Dr. Melville Watson of Toronto who is convener. He represents the demobilized medical officers. As A.D.M.S. of the 3rd Canadian Division, he was Medical Director of the Canadian Assault Force on D-Day. There three members of the Committee, all active practitioners, are devoting four afternoons each week to this work until the completion of the study. The Committee might be regarded as a commission because they plan to hear representations from both groups and individuals.

The extension lectures of the Ontario Medical Association have been extensive and successful since the work began last fall. District meetings and local society meetings were given 79 addresses by 47 speakers. All of the latter save one, Dr. Douglas Taylor, were members of the Faculty of Medicine University of Toronto. Dr. Taylor holds the record as he addressed ten societies. To facilitate the work in the coming year the Association has purchased a kodachrome projector which is more easily portable than the cumbersome lantern formerly used.

The University of Toronto has advertised Advanced Refresher Courses in Medicine, Surgery and Obstetrics and Gynæcology to be held in September. Registration opens April 1 and the classes are restricted to a maximum of 20 in each group. A minimum of seven is required before a course is begun. Those registering early will be sent lists of recommended books and articles for preliminary reading. M. H. V. CAMERON

The following were admitted to Fellowship in the Royal College of Physicians and Surgeons of Canada in 1946.

Fellowship *by examination*: Division of Surgery.—Ernest Gerbert Meyer, Toronto; John Vincent Redman Ord, Toronto; Walter Albert Scott, London; Alexander Gale Shaw, Toronto; Harold V. Slemon, Toronto; George Rutherford Walker, Toronto.

Ad eundem admissions: Division of Surgery.—Dermid Lockhart Cameron Bingham, F.R.C.S.(Edin.), Kingston; Herbert M. Coleman, F.R.C.S.(Edin.), Toronto; Gordon Nelson MacFarlane, F.R.C.S.(Edin.), Sarnia; Jesse Richard Frank Mills, F.R.C.S.(Edin.), Toronto; Hugh Robert Charles Norman, F.R.C.S.(Eng.), Toronto; Edwin Moody Robertson, F.R.C.S.(Edin.), Kingston; James Clifford Samis, F.R.C.S.(Edin.), Ottawa; Frank M. Scott, F.R.C.S.(Edin.), Hamilton; Wallace Beresford Shute, M.R.C.O.G., Ottawa; Burnley Wordlow Stevens, F.R.C.S.(Eng.), Toronto; Ernest Bruce Tovee, F.R.C.S.(Edin.), Toronto; John Clinton Whyte, M.R.C.O.G., Ottawa.

Fellowship *by examination*: Division of Medicine.—Charles Beverly Brown, Toronto; William Bruce Charles, Toronto; Allen Frederic Graham, Toronto; Cameron Coutts Gray, Toronto; Charles H. Jaimet, Hamilton, Ontario; Donald Bernard Moran, Toronto; Donal Patrick Murnaghan, Toronto; John Anthony Gibson Reid, Toronto; Arthur Hunter Squires, Toronto; Ralph Elliott Will, Toronto.

Ad eundem admissions: Division of Medicine.—Francis Staples Brien, M.R.C.P.(Lond.), London; Wilbert Hurst Brown, M.R.C.P.(Lond.), Toronto; William James Gardiner, M.R.C.P.(Lond.), Toronto; Ranald Ian MacDonald, M.R.C.P.(Lond.), Toronto; John William Magladery, M.R.C.P.(Lond.), Toronto; Arthur Ewart Parks, M.R.C.P.(Lond.), Toronto; Alexander A. Roger, M.R.C.P.(Lond.), Toronto; John David Roger, M.R.C.P.(Lond.), Ottawa; George Jasper Wherrett, M.R.C.P.(Lond.), Ottawa.

Quebec

The Women's Medical Society of McGill University celebrated on February 27, the 25th anniversary of the graduation of the first class of women graduates at McGill. The occasion was marked by a dinner at which several members of the Faculty were present. There were 75 women graduates present and Miss W. Kidd of the graduating class was in the chair. Three of the original five women in the graduating class of Medicine '23 were present, Dr. Eleanor Percival, Dr. Mary Childs and Dr. Jessie Scriver. The other two who could not be present were Dr. L. Irwin, now Mrs. J. H. Macdonald and Dr. Winifred Blampin. A specially designed cake was brought in with 25 candles on it, and the three

original graduates performed the ritual of blowing out the candles. After the toasts and their acknowledgment, a presentation was made to Miss G. D. Mudge of the Secretary's office as a mark of esteem and appreciation of her unvarying kindliness to students. Dr. Cushing referred to the revolution in sentiment towards the admission of women to the study of medicine which had taken place during his teaching.

The address for the evening was given by Dr. H. E. MacDermot who showed that women had actually been permitted to practise medicine in the Middle Ages and there are records of some striking personalities amongst women physicians of the time. Then they lost the privilege and did not regain it till Miss Elizabeth Blackwell, in 1847 managed to gain admission to the Medical School of Geneva, N.Y., where she graduated with honours and went on to open the way to the study of medicine by women. McGill was one of the latest to follow the example of other countries in this respect, and it was not until 1918 that the McGill Medical Faculty finally agreed to the arrangement. Maude Abbott had tried in 1890 to gain admission to McGill but the Faculty at that time could not undertake coeducation in medicine. However, the very men who opposed it then eventually changed their minds later on.

L'honorable docteur Paquette, ministre de la Santé, vient d'annoncer que, par suite de la construction de sanatoriums et d'hôpitaux généraux qui seront terminés en 1947, le système d'hospitalisation de la province s'augmentera de plus de 1,985 lits, cette année, dont la moitié pour les tuberculeux.

L'érection de ces maisons d'hospitalisation dans diverses parties de la province a été entreprise l'an dernier et, dans la plupart des cas, les établissements sont sur le point d'être parachevés. Ces hôpitaux et sanatoriums ont été construits avec l'aide de plus de $10,000,000 d'octrois du gouvernement qui, sur l'instigation du docteur Paquette, a entrepris l'exécution d'un vaste programme pour résoudre notre problème d'hospitalisation et répondre à tous les besoins, surtout dans le domaine de la lutte à la tuberculose.

Le ministre de la Santé a parlé d'abord des sanatoriums en voie de construction ou d'agrandissement et qui assureront près de 800 lits de plus, d'ici peu de temps, aux tuberculeux. En voici la liste: Sanatorium de Gaspé: 260 lits; Sanatorium de Sainte-Germaine (Dorchester): 260 lits; Sanatorium Cooke, à Trois-Rivières: construction d'une aile qui lui permettra de recevoir 225 malades de plus; Sanatorium de Mont-Joli (comté Matane): agrandissement projeté qui portera à 620, soit 300 de plus, le nombre de lits.

Vaste sanatorium projeté à Montréal. De plus, le docteur Paquette a déclaré qu'il est en pourparlers avec une communauté religieuse de Montréal, qu'il n'a pas désignée, pour la construction d'un vaste sanatorium de 500 lits destinés aux malades de la région montréalaise. Le ministre croit pouvoir conclure une entente avec cette communauté d'ici la fin du mois. La construction de ce sanatorium, qui porterait à plus de 1,300 le nombre de lits nouveaux pour les tuberculeux, serait entreprise incessamment.

"A mesure que la campagne de dépistage des tuberculeux se fait plus intense, a fait observer le docteur Paquette, le besoin des lits s'accroît. En sorte qu'il s'avèrera probablement urgent que nous procédions en 1947 à la construction d'un deuxième sanatorium de 500 lits, dans le district de Montréal. Si nous pouvons réaliser ce projet, je crois que nous aurons réglé le problème de l'hospitalisation des tuberculeux pour quelque temps à venir."

Lors de la dernière session, le ministère de la Santé a été autorisé par les Chambres à dépenser un montant de $10,000,000 pour intensifier la lutte à la tuberculose. C'est ce qui lui permet de contribuer généreusement à la construction de ces divers sanatoriums.

La lutte à la tuberculose. Cette même loi pourvoyait aussi à la formation d'un comité consultatif chargé de trouver les mesures les plus appropriées pour combattre la tuberculose. Ce comité est en voi de formation et les noms de ses membres seront annoncés dans quelques jours. Ils seront au nombre de neuf, dont trois médecins. Parmi les médecins choisis, il y aura le docteur J.-A. Vidal, directeur des services antituberculeux de la province.

Agrandissement d'hôpitaux. Le docteur Paquette a annoncé ensuite la construction de plusieurs nouveaux hôpitaux et l'agrandissement de certaines autres maisons d'hospitalisation pour les malades, d'une façon générale, avec l'aide du gouvernement. Parmi les hôpitaux qui s'agrandissent, signalons celui de St-François d'Assise, de Québec, dont les travaux sont très avancés et qui pourra recevoir 200 malades de plus.

Un nouvel hôpital est en voie de parachèvement pour la région de Rouyn-Noranda, comté de Témiscamingue, et disposera de 150 lits. Les autres hôpitaux généraux qui se construisent sont les suivants: hôpital de Joliette: 135 lits; hôpital de Sorel: 150 lits; hôpital de St-Eleuthère: 50 lits; hôpital de Sherbrooke (pour les protestants): 100 lits.

A Trois-Rivières, on construit une maternité qui pourra recevoir 200 malades, tandis que l'orphelinat St-Dominique subit un agrandissement qui lui permettra d'hospitaliser 150 enfants de plus.

Le docteur Paquette a déclaré qu'il étudie d'autres projets de construction ou d'agrandissement d'hôpitaux qu'il communiquera bientôt au public, et dont la réalisation sera entreprise et poussée avec rapidité en 1947.

We learn with pleasure that Dr. Adelard Groulx, M.P.H., Director of the Department of Health of the City of Montreal, has recently been honoured by being elected to Fellowship in the American Academy of Pædiatrics. Dr. Groulx's well-known devotedness to the Public Health fully merits the bestowal of this distinction.

Saskatchewan

The College of Physicians and Surgeons of Saskatchewan announce the recent appointment of Dr. G. Gordon Ferguson as Registrar. Dr. Ferguson succeeds the late Dr. J. G. Keber Lindsay.

Dr. Ferguson comes from Moose Jaw where he has been established in private practice since before enlisting in 1940 in the R.C.A.M.C. Major Ferguson was with No. 1 Field Dressing Station when the 1st Canadian Division went into action in Sicily. Following his discharge in 1945 Dr. Ferguson resumed practice in Moose Jaw. He has practised in both rural and urban Saskatchewan.

Born and educated in Winnipeg, he graduated from Manitoba Medical College in 1929. Dr. and Mrs. Ferguson are now in Saskatoon. Their son, Anthony, is attending Ravenscourt School in Winnipeg.

Dr. C. J. Houston of Yorkton succeeds Dr. A. C. Scott of Indian Head as President of the College of Physicians and Surgeons. The membership of the Council is, Dr. R. W. Kirkby of Prince Albert, Dr. J. J. Hamelin of North Battleford, Dr. J. F. C. Anderson of Saskatoon, Dr. C. J. Houston of Yorkton, Dr. J. A. Matheson of Gull Lake, Dr. F. C. Heal of Moose Jaw, Dr. E. A. McCusker of Regina, Dr. M. H. McDonald of Weyburn and Dr. A. C. Scott of Indian Head.

The Saskatchewan Government Hospitalization Plan went into effect January 1, this year. Briefly this plan provides for a complete hospital service, entitling the patient to a standard public ward and including all the services such as x-ray, laboratory, case and operating room, as well as common medications prescribed by the attending physician while in hospital.

All provincial hospitals are filled to capacity and each has a long waiting list. How much of this overcrowding can be blamed on the new plan is still difficult to say since a similar condition existed during the end of last year.

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In Regina Clinical Pathological Conferences are held at the Grey Nuns' Hospital every Saturday during the noon hour. Cases are selected by a program committee from the patients at the Cancer Clinic, as well as the Hospital, and all members are encouraged to present private cases who show interesting features in diagnosis and treatment.

At the Regina General Hospital the scientific part of the program usually follows the monthly meeting. There the material is often drawn from the D.V.A. Wing, but all members of the staff may, and do, present cases under the guidance of the program committee.

On February 18 an exceedingly well attended meeting of the Regina and District Medical Society was held with guests from Moose Jaw, Saskatoon, Indian Head and other points present. Dr. Wallace Wilson, President of the C.M.A., spoke briefly and introduced Dr. T. C. Routley, General Secretary of the C.M.A., who was the main speaker. Dr. Routley gave a very fine talk on the organization and the aims of United Nations Health Organization and the international medical association. He holds great hopes not only for the advancement of medicine but for complete collaboration of medical men of the world to achieve this end.

At the last meeting of the Regina and District Medical Society held on January 31, 1947, Dr. David Rodgers of Regina was the guest speaker. His subject was "Some Adventures in Epidemiology", which covered a series of annual events that he had occasion to deal with overseas in his capacity as medical consultant with the British Medical Services.

Dr. J. W. FitzGerald has recently opened his office in Regina. He confines his practice to Psycho-Somatic Medicine.

Dr. A. M. Longmore has recently joined Dr. D. E. Rodgers in the practice of Internal Medicine in Regina.

B. BRACHMAN

General

The Canadian Tuberculosis Association will hold its annual meeting in Quebec City from May 15 to 17, 1947.

An interesting program has been planned. It includes discussions on streptomycin; pitfalls of mass surveys; rehabilitation of T.B. patients; and T.B. amongst veterans. Clinical meetings will also be held at Laval Hospital.

Hotel reservations should be made early. The Executive Secretary is Dr. Georges Gregoire, 503 Quebec Power Bldg., Quebec.

Canadian Rheumatism Association. — The annual meeting of the Canadian Rheumatism Association will be held in Toronto on Monday, May 12. As well as the annual business meeting, clinical papers will be presented. In view of the reorganization of the Association since the war, will former members of the Association wishing to remain active please forward the annual fee of $2.00 to the Secretary-Treasurer, Dr. W. S. Barnhart, Medical Arts Building, Ottawa.

The convention of the **Canadian Society of Laboratory Technologists** to be held in May, 1947, will be the 10th anniversary of the incorporation of the C.S.L.T. under Dominion Charter in 1937. It will be held at the Royal Connaught Hotel, Hamilton, Ontario, on May 29, 30, and 31, 1947. Guests (non-members) will be welcome at all but the business sessions. Papers and scientific movies on various aspects of laboratory technique will be presented. For further information write to Miss Helen L. Smith, Secretary Canadian Society of Laboratory Technologists, 294 Barton St. E., Hamilton, Ontario.

The American Association of Obstetricians, Gynæcologists and Abdominal Surgeons announces a foundation prize contest.

For further information write Dr. James R. Bloss, Secretary, 418 Eleventh Street, Huntington 1, West Virginia.

The 30th annual meeting of the **American Dietetic Association** will be held in Philadelphia, October 13 to 17, 1947. The Philadelphia Convention Hall will house the exhibits and meetings.

The Medical Library Association will hold its forty-sixth Annual Meeting in Cleveland, Ohio, May 27 to 29, at the invitation of the Cleveland Medical Library Association, with headquarters at the Wade Park Manor.

The scientific sessions on May 27 and 28 will include papers by several members of the Association on varied subjects of interest to medical and dental librarians, each paper to be followed by a short discussion period. Dr. Morris Fishbein will be the guest speaker at the Banquet to be held Tuesday evening, May 27.

The Wednesday, May 28, afternoon meeting will be devoted to a "Symposium on Visual Aids and the Medical Library".

Further information will be available from the Secretary, Miss Heath Babcock, New York State Medical Library, Albany 1, N.Y.

We have received a copy of the brochure summarizing the history of the first 100 years of the New York Academy of Medicine. The booklet is a striking little pamphlet and contains much interesting detail on the growth of the Academy. A very full program has been arranged in connection with this centenary.

A new Society, called the **Canadian Otolaryngological Society**, was organized at the Banff meeting in 1946.

This Society has been formed with the object of aiding the study of otolaryngological problems in relation to public welfare and health, and of promoting the interests of otolaryngologists throughout Canada. The first annual meeting will be held on June 23 and 24 at Minaki Lodge, Ontario.

The officers of this Society are: Dr. G. E. Hodge, President, Montreal; Dr. Howard McCart, Vice-president, Toronto; Dr. E. J. Washington, Treasurer, Winnipeg; Dr. Jules Brahy, Secretary, Montreal.

Training of X-ray Technicians—Survey by Canadian Association of Radiologists. — The Canadian Association of Radiologists is conducting among its membership and among the hospitals in which Radiologists are working a survey pertaining to the courses of instruction that are being given to x-ray technicians in Canada.

The Canadian Society of Radiological Technicians conducts examinations twice a year for the Certification of Registered X-Ray Technicians, but with the exception of the large centres in Canada, there are few facilities available for the instruction of candidates for these examinations. At present, there is a shortage of trained x-ray technicians and with the increasing demands upon x-ray departments, the situation throughout the country has become of considerable concern to radiologists. The Canadian Society of Radiological Technicians and the Provincial Societies of Radiological Technicians are anxious to establish proper standards and qualifications, and it is in the interest of medicine in Canada that these qualifications become known. At the moment there are a number of people being employed as x-ray technicians who do not, and some of them can not, meet the required standards.

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BOOK REVIEWS

Urologic Roentgenology. M. B. Wesson, Ex-President American Urological Association. 259 pp., illust., 2nd ed. $5.50. Lea & Febiger, Philadelphia; Macmillan Co. of Canada, Toronto, 1946.

The advances in urologic roentgenology and refinements of radiological technique in recent years, prompted the author to prepare this second edition of his work. It comprises a collection of excellent urological films, drawn from leading clinics in America. The presentation of concise case history captions, with pathological confirmation of diagnoses makes this volume most attractive. It is not intended as a highly specialized treatise, but is of value both to the general medical public, and the urologist. The pitfalls in diagnosis are well illustrated, and emphasis is placed on the possibility of error in interpretation of pyelograms. The author has included a section on Arteriography, a relatively new field in renal visualization, which appears to offer rather limited possibilities as a diagnostic measure in urology. Frequent diagrammatic, or actual pictorial plates of pathological lesions accompany the pyelograms, and enable one to correlate the roentgenologic findings with the disease process involved. The bibliography has been brought up to date, and affords ready access to references, elaborating the many urological conditions presented. With the more extensive use of urography in modern medical practice, a volume of this nature serves a real need, and should be well received by the profession.

Dermatology for Nurses. K. A. Baird, M.A., M.D., C.M., F.A.C.A. 63 pp., illust. $2.00. The Ryerson Press, Toronto, 1946.

This little book is attractively written and will be of undoubted help to nurses in training. It avoids conventional classifications and puts no burden on the student nurse who can hardly be expected to acquire the extensive nomenclature of dermatology. Skin diseases are considered as reactions to one or more of three types of offenders. (1) Living offenders; parasites of bacteria. (2) Physical offenders; mechanical and forces like heat, cold, electricity and x-ray. (3) Chemical substances; externally applied and endogenous.

General principles of treatment are offered for each class of offenders and the basic principles of allergy are discussed. Eleven full page photographs illustrate as many common diseases of the skin.

Eye Manifestations of Internal Diseases. I. S. Tassman, Associate Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania, Philadelphia. 614 pp., illust., 2nd ed. $11.00. The C. V. Mosby Co., St. Louis; McAinsh & Co., Ltd., Toronto, 1946.

As the author states in his preface, the first five chapters are intended for "student beginners"; one might go further and state that the substance of the first part is too elementary for practising oculists, and too detailed for most physicians and surgeons, but is ideal background for the young surgeon starting his internship in ophthalmology, or for the general practitioner who must do a bit of ophthalmology in his practice.

The main body of the book (chapters VI *et seq.*) is a real contribution from two points of view; firstly, to remind the ophthalmologist of the general or systemic diseases which are in part manifesting themselves in the eye, and secondly to enable the internist to know what to seek in the eye. In this way the book serves as a handy reference. An important feature of every reference book is a good index; where other books have fallen down in this respect, Tassman has made it very easy to find a desired topic.

The book follows closely upon the 1942 edition in the manner of presentation; in the matter of detail, it has been brought up to date by the addition of new syndromes and diseases, both as regards etiology and therapy.

Modern Treatment of Diabetes Mellitus. W. S. Collens, Chief of the Diabetic Clinic, Israel Zion Hospital, Brooklyn, and L. C. Boas, Assistant in the Diabetic Clinic, Israel Zion Hospital, Brooklyn. 514 pp., illust. $8.50. Charles C. Thomas, Springfield, Ill.; Ryerson Press, Toronto, 1946.

This book has obviously been written as a guide to general practitioners who treat diabetics and is not intended to be a manual for the patient. It deals with the historical aspect of the disease, diagnosis, classification of patients, treatment by diet and insulin and the complications which occur in diabetics. Included with the book is a "Collens Diet Calculator". With this calculator one can prescribe a menu for various diet formulæ with different ratios of carbohydrate, fat and protein.

The authors, for the most part, adhere to the school which favours a moderate carbohydrate, moderate fat, and moderate protein diet. There are some investigators of diabetes who will differ with the authors on this point. Many will prefer lower fat intakes and higher protein intakes than those recommended. The chapter on the treatment of diabetic coma is open to criticism. In the opinion of the reviewer the amounts of insulin advocated are too small and also the administration of glucose should not be commenced until the level of the blood sugar is approaching normal. The authors advocate the use of alkali therapy. This is certainly a controversial point, and it is unfortunate that the scope of the book does not permit publication of data in support of their contentions. The work on degenerative disease of the peripheral arteries is excellent and the use of coloured photographs adds considerably to the value of this section. The chapters on the methods of insulin administration and urinalysis are good, but that on the technique of blood chemistry is too sketchy to be of value and in any case is not necessary in a book of this type.

Neurology and Psychiatry for Nurses. Frederick P. Moersch, Professor of Neurology, Mayo Foundation, Rochester, Minnesota. 176 pp., illust., 3rd ed. revised. $1.75. Burgess Publishing Co., Minneapolis 15, Min.

This is the third edition of a very valuable and inexpensive book dealing with these subjects from the nurse's standpoint. The language is simple and practically all diseases of the nervous system are discussed briefly. The section on psychiatry and mental hygiene is nicely arranged and a short review of the history of psychiatry is included. This edition has been much improved by the use of some excellent illustrations and much new material has been added since the last edition. In the reviewer's experience, all nurses who have read the book have been impressed with the simplicity of the language and its usefulness to them in their work. It may be considered a necessary book for the library of nurses in training schools, and the graduate nurses studying neurology and psychiatry will find it a valuable addition to their library.

Nature of Disease up to Date. J. E. R. McDonagh, F.R.C.S. 168 pp., illust. 15s. Messrs. William Heinemann Medical Books Limited, London, 1946.

In 1940 the reviewer attempted to understand a large book by this author entitled The Universe Through Medicine. Some forty years of research have gone into this work and out of it has come the Nature of Disease Institute to which body the author reports annually. It seems that the Institute stands for a unitary theory of disease and works back to a principle that a healthy soil producing perfect food would preserve men and animals in health. The sap in plants and the blood in men and beasts inhibit the variations in a hypothetical rhythm of expansion and contraction of protein mole-

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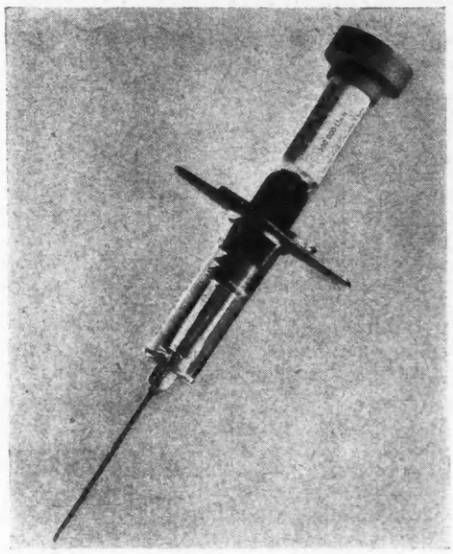
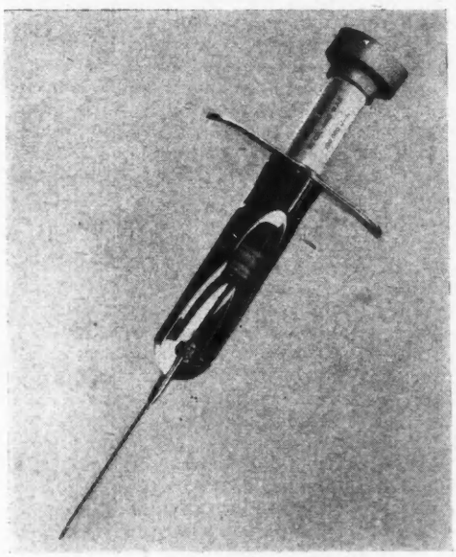


Disposable Plastic Syringe



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cules. Activity may be modified in many ways. Abnormalities of rhythm constitute disease and modifiers of one set or another may restore a normal pulsation. Apparently the author believes in metamorphosis of organisms such as the changing of Döderlen's Bacillus into spirillæ and spirochætæ. He also approves homœopathic potentizing and argues against pasteurization of milk.

It has taken the author a long time to create his hypothesis. It will take a long time for orthodox physicians to understand the theory. The philosophically minded doctor should read this book and wait the revelation it may contain. Psalm 139 has a summary of this review "such knowledge is too wonderful for me!"

Skin Diseases in Children. G. M. MacKee, Professor of Clinical Dermatology and Syphilology, New York Post-Graduate Medical School, Columbia University; A. C. Cipollaro, Associate in Dermatology and Syphilology, New York Post-Graduate Medical School, Columbia University. 448 pp., illust., 2nd ed. $7.50. Paul B. Hoeber, Inc., New York, 1946.

The second edition of this book is easily read and contains the practical information only to be obtained from dermatologists of wide experience. The few coloured photographs are not good, the black and white photographs are, for the most part, excellent, though some would be of little value to one not familiar with diseases of the skin.

Sulfa drugs used topically and penicillin used topically or intramuscularly, have not proved so valuable as one would imply. Probably the book was written before there was sufficient time for further observation of treated patients. Too little is said about the bad secondary effects of sulfa drugs used locally though we agree that these effects are less common in children than in adults. Penicillin used locally or intramuscularly does not cure sycosis vulgaris as one would gather from the text.

There is a section describing the various contagious diseases not always found in a textbook of dermatology. This will prove of value in differential diagnosis. The book should be popular. It is a distinct contribution to dermatology.

Gastroenterology in General Practice. L. Pelner, Associate Attending Physician, Greenpoint Hospital, Brooklyn, New York. 285 pp., illust. $9.50. Charles C. Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1946.

In the preface it is suggested that this work is offered as a hand-book which general practitioners especially will find useful. It is a sort of bird's-eye view of digestive disturbances including not only those which arise from the alimentary canal but also those traceable to the ancillary organs of digestion. A great amount of helpful information has been crowded into 260 pages and numerous figures and illustrations—20 of which are colour plates—do much to lessen the obscurity which almost necessarily attends such an abbreviated text. Despite the illustrations, the meaning is occasionally not clear but on the whole the general reader will not often be in serious difficulty from vagueness in the writing or because of the omission of important or relevant facts.

As long as he is dealing with established or accepted beliefs, the author is usually not glaringly in error. When he gives recommendations about methods of investigation or opinions on therapy he is a less reliable guide. In an off-hand way, he advises time-consuming and costly examinations—such as x-ray and gastroscopy twice yearly in patients with pernicious anæmia—which, though possibly valuable for record purposes, cause annoyance and frequently financial worry to patients of average means. He seems to forget or disregard a fundamental principle of dyspeptic therapy—the avoidance of all forms of irritation.

The book is enlarged, though perhaps not improved, by reports on some excursions made by the author into psycho-somatic medicine. Because the emotions are often complicating factors in dyspepsia, the genuine gastroenterologist early learns to keep on solid ground. He is likely to be something less than pleased to find that his chosen field is becoming an area for the psychoanalyst.

Pharmacology and Therapeutics. A. R. Cushny, Late Professor of Materia Medica and Pharmacology in the University of Edinburgh. Revised by A. Grollman, Professor of Medicine and Chairman of the department of experimental medicine, the Southwestern Medical College; and D. Slaughter, Dean of the Medical School, University of South Dakota. 868 pp., illust., 13th ed. $8.50. Lea & Febiger, Philadelphia; Macmillan Co. of Canada, Toronto, 1947.

The present editors of this classic have done well to follow so closely the excellent arrangement with which we have become so familiar in "Cushny". It is difficult to add to the repeated acknowledgment of the hight quality of this textbook. Naturally one looks to see how the latest therapeutic advances are dealt with. They are all there, up to and including streptomycin and the caution as to the ease with which resistance to it may be developed. There are also short references to other less well known antibiotics.

The book still performs admirably its function as a guide both to student and to practitioner rather than as a compendium of pharmacological knowledge.

Human Genetics. Vol. I. R. R. Gates, Emeritus Professor of Botany in the University of London. 753 pp., illust. Vol. II. 775 pp., illust. $15.00 per set. Macmillan Co., New York, Macmillan Co. of Canada, Toronto, 1946.

This work is an encyclopædia, rather than a text of human genetics for students. Most of the important references in the field of human genetics are probably included in the some 5,600 references which the work contains. With such a comprehensive work, it is inevitable that mistakes should creep in, or that the reader would wish for some different arrangement of material. One suggestion for arranging the bibliography in future editions is offered. All references should be alphabetically arranged at the end of the second volume. This will obviate the replication of some references, which have crept in five or six times after different chapters, and the unfortunate omission of others, which have been mentioned in the text, but omitted in the bibliography of any chapter.

There are 90 pages of index, with many cross references and detailed subheadings which make for ready finding of most subjects which the book discusses. Despite the full indexing, however, there are points in which this could be improved; for example, cervical ribs, if discussed, are not under the heading of "ribs" or "cervical"; chronic œdema is not under the heading of œdema or chronic œdema, but under "disease"; imperforate anus is not under intestine, or anus, but "atresia". The reviewer has not discovered under what heading congenital dislocation of the hip is discussed; it is not under "hip", or "dislocation". An even fuller indexing, with the topic discussed under the main anatomical region involved, as well as under other names, would make for readier reference.

The reviewer wishes that in the text a more critical attitude could be taken by the author with respect to certain items. For example when a group of individuals in a family shows 23 affected and 24 normal, the text states that the defect is "strictly dominant". When the numbers of affected and normal are not so obviously evenly apportioned, the defect may be just as "strictly dominant", but the text does not lead the reader to feel that the inheritance is so clear cut as in the first instance. In one instance the expectation was a 3-affected-to-1-normal ratio, and the text pointed out that in one family the number of affected was 4 and of normal was 6. The inference is that this family was not agreeing with theoretical expectation. As a matter of fact, so much departure from a 3:1 ratio as was exhibited by this family is to be expected

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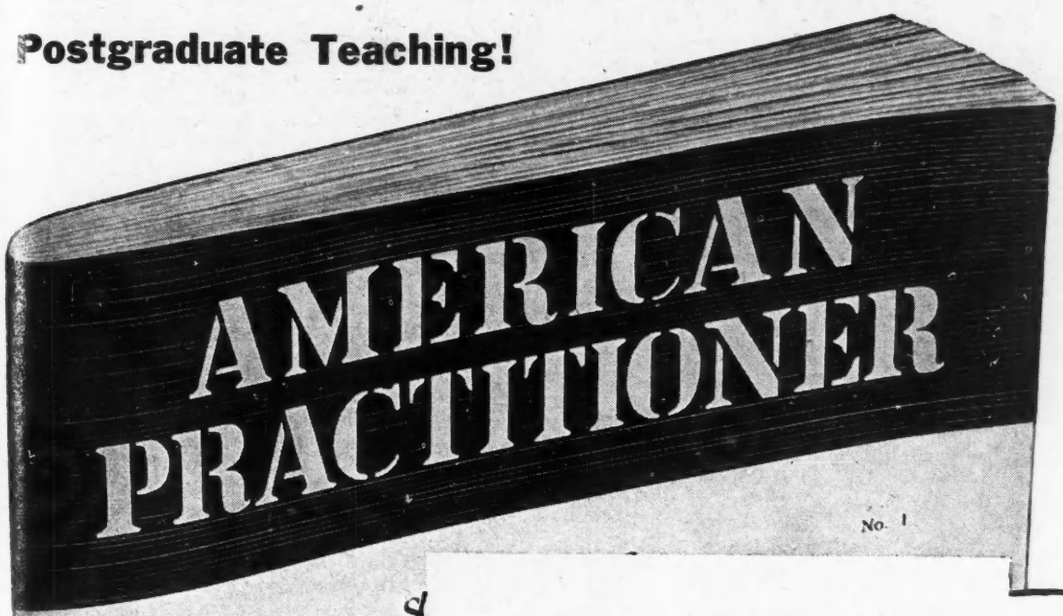

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in one-seventh of all such families. The author should add after such statements the comment that such departure from theoretical expectations is well within normal limits of variation or that it is outside such limits as the case may be; thus affording the reader who is not likely to be nearly so well acquainted with these facts as is Professor Gates, an idea as to whether such departure from expectation destroys the idea that the defect is behaving as a dominant or a recessive in the family in question.

Despite inaccuracies in places, despite the unfortunate misunderstanding of gene frequencies and the types of persons expected in each group, as evidenced by confusion on the section on blood groups, despite the omission of the recent methods of analysis of human hereditary traits, the book is a valuable compilation of material, and puts together in accessible form most of what is known about inheritance of human traits.

In the first volume, following the introductory chapter, there are chapters dealing with general Principles of Heredity in Man; Human Cytology; Linkage; Eye and Hair Colour; Colour Blindness; Defects and Diseases of the Eye; Ear, Skin, Hair, Nails and Teeth; Albinism; Defects in Hands and Feet; Skeleton; Metabolism; Diseases of the Blood, and Blood Vessels, Hæmophilia; Blood Groups. In Volume 2, the topics discussed are Allergy, various hereditary syndromes, such as Morquio's, Gargolyism, etc.; Diseases of the Alimentary Tract; Reproductive System; Twins; Diseases of the Muscular System; of the Nervous System; Mental Defects; Normal Mental Differences; Cancer; Constitution; Congenital Anomalies; Stature; Anthropological Charatcers; and a group of miscellaneous traits.

The book is well done from the standpoint of the printing job, the type being clear, the typographical errors at a minimum, the illustrations good. The publishers are to be congratulated on having published this work, and on having made available to the public a storehouse of information not available under one cover in any other publication. The author is to be congratulated for having so successfully completed what was a most arduous task, and one which no one would have undertaken except as a labour of love.

BOOKS RECEIVED

Use of Research by Professional Associations in Determining Program and Policy. E. L. Brown, Drector, Department of Studies in the Professions, Russell Sage Foundation. 39 pp. $0.25. Russell Sage Foundation, New York, 1946.

1946 Year Book of General Medicine. Edited by G. F. Dick, Professor of Medicine, University of Chicago; J. B. Amberson, Professor of Medicine, College of Physiciasn and Surgeons, Columbia University; G. R. Minot, Professor of Medicine, Harvard University; Wm. B. Castle, Professor of Medicine, Harvard University; Wm. D. Stroud, Professor of Cardiology, Graduate School of Medicine, University of Pennsylvania; G. B. Eusterman, Professor of Medicine, University of Minnesota (Mayo Foundation). 772 pp., illust. $3.75. Year Book Publishers, Inc., Chicago, 1946.

Chemotherapeutic and Other Studies of Typhus. M. Van Den Ende, C. H. Stuart-Harris, F. Fulton and J. S. F. Niven, with C. H. Andrewes, A. M. Begg, W. J. Elford, M. H. Gleeson White, W. L. Hawley, K. C. Mills, F. Hamilton and C. C. Thomas. Medical Research Council Series No. 255. 255 pp., illust. 12s. 6d. His Majesty's Stationery Office, London, 1946.

Clinics. Vol. V, No. 3. Edited by G. M. Piersol, Professor of Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia. 179 pp., illust. $2.00. J. B. Lippincott Co., Philadelphia, Pa., October, 1946.

Lehrbuch der Urologie. J. Minder, Ehem. Ordinarius der Urologie und Direktor der Urolog. Universitats-Klinik Budapest zur Zeit Specialarzt der Urologie in Zurich. 348 pp., illust. Fr. S. 37.50. Medizinischer Verlag Hans Huber, Bern; Grune & Stratton Inc., New York, 1946.

Medical Annual, 1946. Edited by Sir Henry Tidy and A. R. Short. 583 pp., illust. $6.75. John Wright & Sons Limited, Bristol; Macmillan Co. of Canada, Toronto, 1946.

Metabolic Therapy of Cancer. E. Freund, former Professor of Pathological Chemistry, University of Vienna. Translated by L. Wolfe. 178 pp. Daniel Godwin Ltd., London, 1946.

Military Neuropsychiatry. Proceedings of the Association for Research in Nervous and Mental Disease, December 15 and 16, 1944. Vol. XXV. 366 pp., illust. The Williams & Wilkins Co., Baltimore; The University of Toronto Press, Toronto, 1946.

Outline of the Spinal Nerves. J. Favill, Clinical Professor of Neurology (Rush), University of Illinois College of Medicine. 191 pp., illust. $4.50. Charles C. Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1946.

Rheumatism and Backaches. J. D. Wassersug, Teaching Assistant in the Outpatient Department of the Boston City Hospital. 310 pp. $2.50. Wilfred Funk, Inc., New York, 1947.

Story of Human Birth. A. F. Guttmacher, Associate Professor of Obstetrics, Johns Hopkins University. 214 pp., illust. 25c. First published by the Viking Press under the title of "Into this Universe". Penguin Books, Inc., New York, 1947.

Textbook of Bacteriology. R. W. Fairbrother, Director of the Department of Clinical Pathology, Manchester Royal Infirmary. 480 pp., illust., 5th ed. 17s. 6. Messrs. William Heinemann Medical Books Ltd., London, 1946.

ACCIDENT IN A DOCTOR'S HOUSE—A Glasgow radiologist, having advised a patient, asked him to let himself out. Some time later the patient was found lying on the basement stairs with a broken spine; he died two weeks later, and his widow and eight children were awarded £1,641 damages by the Court of Session in Edinburgh. Their Lordships found that the passage through which the patient had had to go was dark or badly lit, and that the nearness of the unlighted basement stairs constituted a danger to a person not acquainted with the house; they therefore held that the doctor had been negligent. The law of England and Scotland alike makes the owner of premises liable to take all reasonable steps to protect a person who comes on to the premises by invitation, and a patient visiting a doctor would fall into this category. The Court's judgment was, however, upset on appeal. Lord Cooper, the Lord Justice-Clerk, found on the evidence that the stair light had been lit and the door open. It could not have been foreseen that any normal person seeking to go out would turn away from the lighted portion of the premises in order to explore, unaided, the unlit portions of a strange house. The doctor had no duty to foresee the unaccountable conduct of the deceased, who was himself the author of his fatal misfortune.—*Brit. M. J.*, May 11, 1946.